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NEWS 2	APR 04	STN AnaVist, Version 1, to be discontinued
NEWS 3	APR 15	WPIDS, WPINDEX, and WPIX enhanced with new predefined hit display formats
NEWS 4	APR 28	EMBASE Controlled Term thesaurus enhanced
NEWS 5	APR 28	IMSRESEARCH reloaded with enhancements
NEWS 6	MAY 30	INPAFAMDB now available on STN for patent family searching
NEWS 7	MAY 30	DGENE, PCTGEN, and USGENE enhanced with new homology sequence search option
NEWS 8	JUN 06	EPFULL enhanced with 260,000 English abstracts
NEWS 9	JUN 06	KOREAPAT updated with 41,000 documents
NEWS 10	JUN 13	USPATFULL and USPAT2 updated with 11-character patent numbers for U.S. applications
NEWS 11	JUN 19	CAS REGISTRY includes selected substances from web-based collections
NEWS 12	JUN 25	CA/CAplus and USPAT databases updated with IPC reclassification data
NEWS 13	JUN 30	AEROSPACE enhanced with more than 1 million U.S. patent records
NEWS 14	JUN 30	EMBASE, EMBAL, and LEMBASE updated with additional options to display authors and affiliated organizations
NEWS 15	JUN 30	STN on the Web enhanced with new STN AnaVist Assistant and BLAST plug-in
NEWS 16	JUN 30	STN AnaVist enhanced with database content from EPFULL
NEWS 17	JUL 28	CA/CAplus patent coverage enhanced
NEWS 18	JUL 28	EPFULL enhanced with additional legal status information from the epoline Register
NEWS 19	JUL 28	IFICDB, IFIPAT, and IFIUDB reloaded with enhancements
NEWS 20	JUL 28	STN Viewer performance improved
NEWS 21	AUG 01	INPADOCDB and INPAFAMDB coverage enhanced
NEWS 22	AUG 13	CA/CAplus enhanced with printed Chemical Abstracts page images from 1967-1998
NEWS 23	AUG 15	CAOLD to be discontinued on December 31, 2008
NEWS 24	AUG 15	CAplus currency for Korean patents enhanced
NEWS 25	AUG 25	CA/CAplus, CASREACT, and IFI and USPAT databases enhanced for more flexible patent number searching
NEWS 26	AUG 27	CAS definition of basic patents expanded to ensure comprehensive access to substance and sequence information

<12/04/2007> Erich Leese

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 NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
              AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

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* * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 16:01:16 ON 15 SEP 2008

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                                                         ENTRY    SESSION
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DICTIONARY FILE UPDATES:  14 SEP 2008  HIGHEST RN 1049627-95-3

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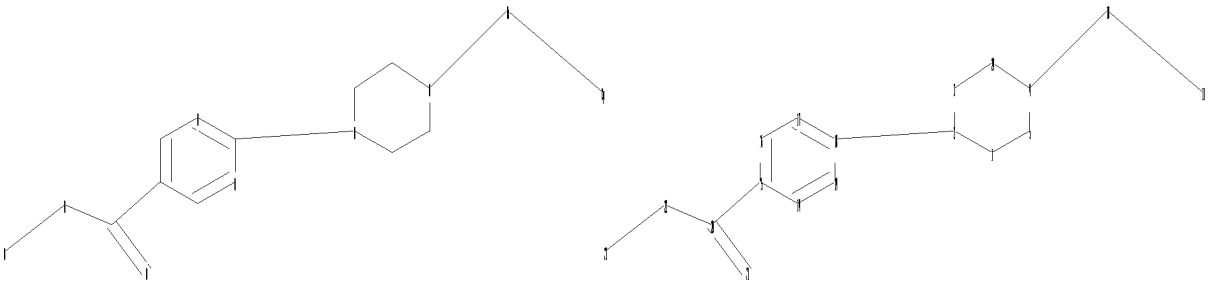


chain nodes :
10 11 20 21 22 23
ring nodes :
1 2 3 4 5 14 15 16 17 18 19 24
chain bonds :
2-18 4-10 10-11 15-20 20-21 20-22 22-23
ring bonds :
1-2 1-5 2-3 3-24 4-5 4-24 14-15 14-19 15-16 16-17 17-18 18-19
exact/norm bonds :
1-2 1-5 2-3 2-18 3-24 4-10 4-5 4-24 10-11 20-21 20-22 22-23
exact bonds :
15-20
normalized bonds :
14-15 14-19 15-16 16-17 17-18 18-19
isolated ring systems :
containing 1 :

G1:C,N

G2:Ak,NH2,NO2

G3:O

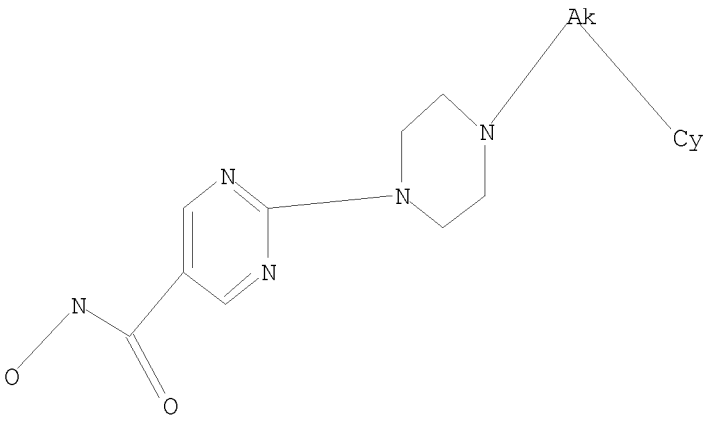
G4

G5:C,N,Zn,H

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 10:CLASS 11:Atom 14:Atom 15:Atom
16:Atom 17:Atom 18:Atom 19:Atom 20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:Atom

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



G1 C,N

G2 Ak,NH2,NO2

G3 O

G4

G5 C,N,Zn,H

Structure attributes must be viewed using STN Express query preparation.

=> s l1 full
FULL SEARCH INITIATED 16:01:46 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 1679 TO ITERATE

100.0% PROCESSED 1679 ITERATIONS 113 ANSWERS
SEARCH TIME: 00.00.01

L2 113 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	178.36	178.57

FILE 'CAPLUS' ENTERED AT 16:01:51 ON 15 SEP 2008
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FILE COVERS 1907 - 15 Sep 2008 VOL 149 ISS 12
FILE LAST UPDATED: 14 Sep 2008 (20080914/ED)

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reclassification data for the second quarter of 2008.

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/legal/infopolicy.html

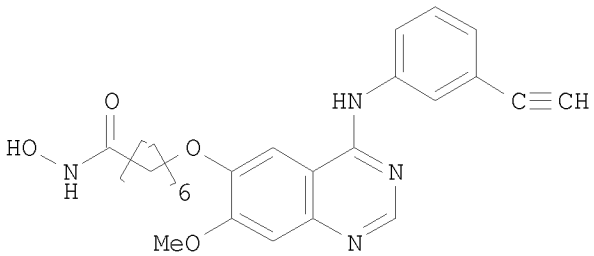
=> s l2 full
L3   11 L2

=> d ibib abs hitstr tot

L3 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:353001 CAPLUS
DOCUMENT NUMBER: 148:355828
TITLE: Multi-functional small molecules as anti-proliferative agents and their preparation
INVENTOR(S): Cai, Xiong; Qian, Changgeng; Gould, Stephen; Zhai, Haixiao
PATENT ASSIGNEE(S): Curis, Inc., USA
SOURCE: PCT Int. Appl., 494pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008033747	A2	20080320	WO 2007-US77971	20070910
WO 2008033747	A9	20080724		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
US 20080221132	A1	20080911	US 2007-852458	20070910
PRIORITY APPLN. INFO.:			US 2006-843590P	P 20060911
			US 2007-895889P	P 20070320

OTHER SOURCE(S): MARPAT 148:355828
GI



A—B—C I II

AB The invention relates to the compns., methods, and applications of an approach to selective inhibition of several cellular or mol. targets with a single small mol. More specifically, the present invention relates to multi-functional small mols. of formula I wherein one functionality is capable of inhibiting histone deacetylases (HDAC) and the other functionality is capable of inhibiting a different cellular or mol. pathway involved in aberrant cell proliferation, differentiation or

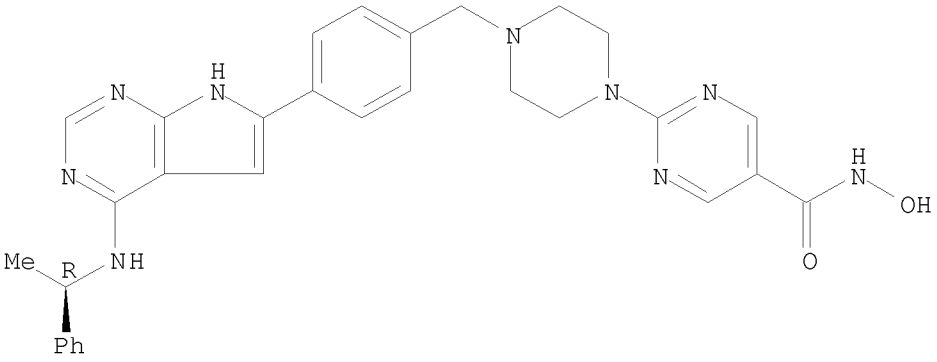
survival. Compds. of formula I wherein A is a pharmacophore of an anticancer agent capable of inhibiting at least one cellular or mol. pathway involved in the aberrant cell proliferation, differentiation or survival; B is a linker; C is a zinc-binding moiety; and their geometrical isomers, enantiomers, diastereoisomers, racemates, pharmaceutically acceptable salts, prodrugs and solvates thereof, are claimed. Example compound II was prepared by a multistep procedure (procedure given). All the invention compds. were evaluated for their antiproliferative activity (some data given).

IT 1011716-90-7P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRPH (Prophetic); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prophetic starting material; preparation of multi-functional small mols. as antiproliferative agents)

RN 1011716-90-7 CAPLUS

CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[4-[4-[[(1R)-1-phenylethyl]amino]-7H-pyrrolo[2,3-d]pyrimidin-6-yl]phenyl]methyl]-1-piperazinyl]- (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:351928 CAPLUS
DOCUMENT NUMBER: 148:355814
TITLE: Preparation of (aralkylamino)(phenyl)pyrrolo[2,3-d]pyrimidine derivatives for use as protein tyrosine kinase (PTK) inhibitors
INVENTOR(S): Cai, Xiong; Qian, Changgeng; Gould, Stephen
PATENT ASSIGNEE(S): Curis, Inc., USA
SOURCE: PCT Int. Appl., 123pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008033745	A2	20080320	WO 2007-US77968	20070910
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 20080161320	A1	20080703	US 2007-852440	20070910
PRIORITY APPLN. INFO.:			US 2006-843646P P	20060911
			US 2007-895894P P	20070320

OTHER SOURCE(S): MARPAT 148:355814
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

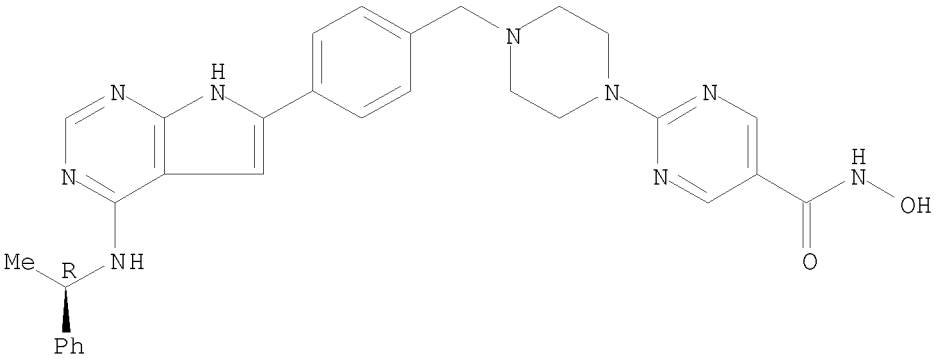
AB Fused bicyclic pyrimidine derivs. I and II [Ar = aryl, substituted arylheteroaryl or heteroaryl; Q = absent or (un)substituted alkyl; X = O, S, NH, or alkylamino; Z = O, S, NR1; Y = N or CR2; B = linker; D = C(O)NH2, NHC(S)CH3, CHC(O)NHacyl, etc.; R1 = H or (un)substituted alkyl; R2 = H, halo, (un)substituted aliphatic, aryl or heteroaryl], and their pharmaceutically acceptable salts, are prepared and disclosed as protein tyrosine kinase (PTK) inhibitors. Thus, e.g., III was prepared by N-alkylation of 1,4-dioxa-8-azaspiro[4.5]decane with 6-(4-(chloromethyl)phenyl)-N-((R)-1-phenylethyl)-7H-pyrrolo[2,3-d]pyrimidin-4-amine (preparation given) and deprotection followed by condensation with 6-aminohexanoic acid Me ester and amidation with hydroxylamine. Select I were evaluated in EGFR assays, e.g., III demonstrated an IC50 value of ≤0.1 (μM).
IT 1011716-90-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(preparation of (aralkylamino)(phenyl)pyrrolopyrimidine derivs. for use as protein tyrosine kinase (PTK) inhibitors)

RN 1011716-90-7 CAPLUS

CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[4-[4-[[(1R)-1-phenylethyl]amino]-7H-pyrrolo[2,3-d]pyrimidin-6-yl]phenyl]methyl]-1-piperazinyl]- (CA INDEX NAME)

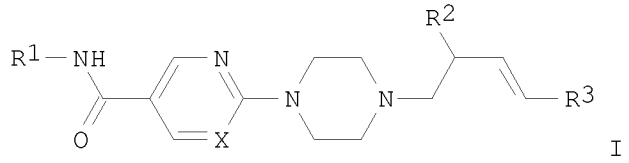
Absolute stereochemistry.



L3 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:816930 CAPLUS
DOCUMENT NUMBER: 147:211903
TITLE: Preparation of pyrimidine derivatives as histone deacetylase inhibitors
INVENTOR(S): Marconnet-Decrane, Laurence Francoise Bernadette; Gaurrand, Sandrine Francoise Dominique; Angibaud, Patrick Rene
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 62pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2007082874	A1	20070726	WO 2007-EP50371		20070116
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW					
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
CA 2630717	A1	20070726	CA 2007-2630717		20070116
PRIORITY APPLN. INFO.:			EP 2006-100570	A	20060119
			WO 2007-EP50371	W	20070116

OTHER SOURCE(S): MARPAT 147:211903
GI



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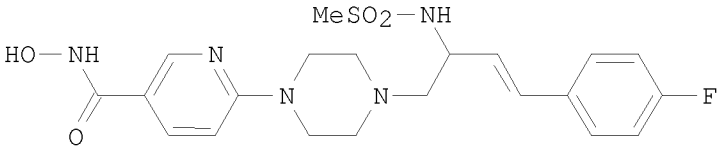

F_3CCO_2H II

<12/04/2007> Erich Leese

AB The title compds. with general formula I [wherein R1 = OH or substituted phenyl; X = N or CH; R2 = amino, alkylamino, alkoxyl, OH, etc.; R3 = (un)substituted Ph, naphthalene, or heterocycle] or N-oxide forms, pharmaceutically acceptable salts, or stereoisomeric forms thereof were prepared as histone deacetylase (HDAC) inhibitors for the treatment of proliferative diseases. For example, compound II was prepared in a multi-step synthesis. In vitro assay for inhibition of HDAC was performed to measure the inhibition of HDAC enzymic activity, and colorimetric assay was performed to determine cellular activity on A2780 tumor cells. II showed HDAC inhibitory and anti-proliferative activities in the above two assays with pIC50 values of 7.0 and 5.3, resp. Formulations containing I as active ingredients were also reported.

IT 944738-91-4P 944738-94-7P 944738-97-0P
944739-00-8P 944739-08-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyrimidine derivs. as histone deacetylase inhibitors)

RN 944738-91-4 CAPLUS

CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-(acetylamino)-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 944738-90-3
CMF C21 H26 N6 O3

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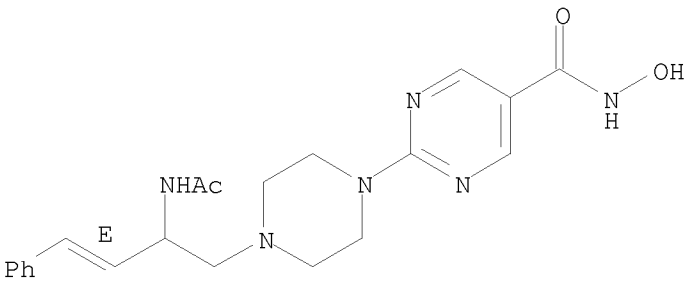

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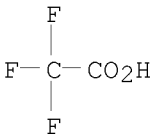
CRN 76-05-1
CMF C2 H F3 O2

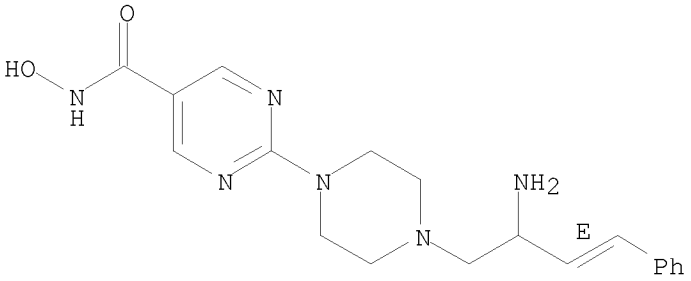


RN 944738-94-7 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-amino-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 944738-93-6
CMF C19 H24 N6 O2

Double bond geometry as shown.



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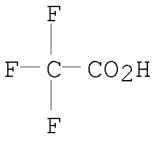
CRN 76-05-1
CMF C2 H F3 O2

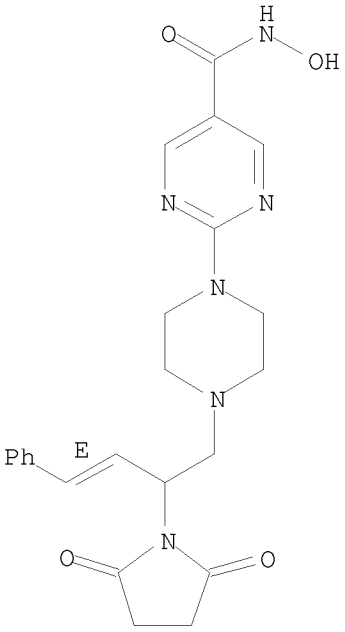


RN 944738-97-0 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-(2,5-dioxo-1-pyrrolidinyl)-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

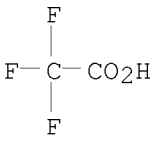
CRN 944738-96-9
CMF C23 H26 N6 O4

Double bond geometry as shown.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

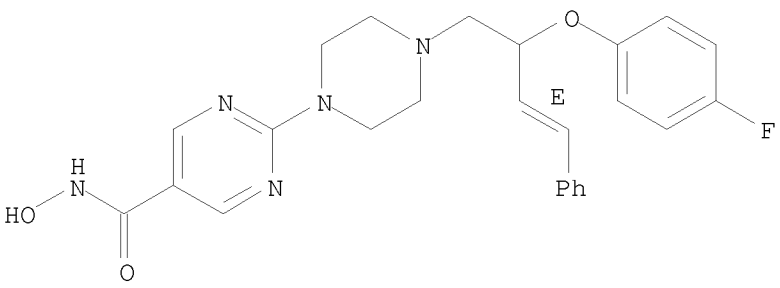


RN 944739-00-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-(4-fluorophenoxy)-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 944738-99-2
CMF C25 H26 F N5 O3

Double bond geometry as shown.



CM 2

CRN 76-05-1
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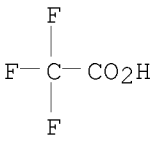
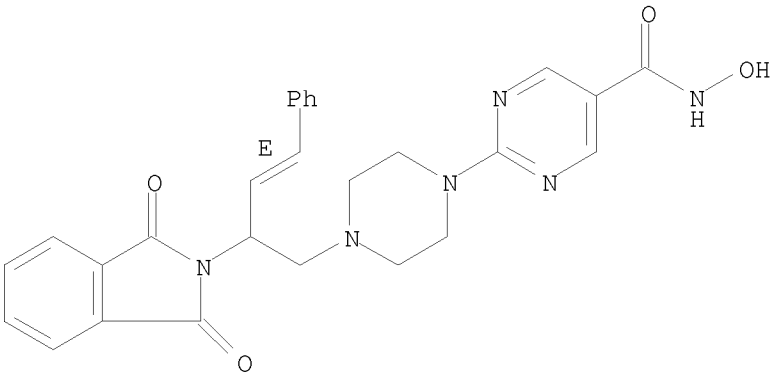


RN 944739-08-6 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

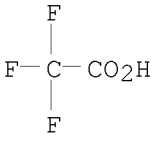
CRN 944739-07-5
CMF C27 H26 N6 O4

Double bond geometry as shown.



CM 2

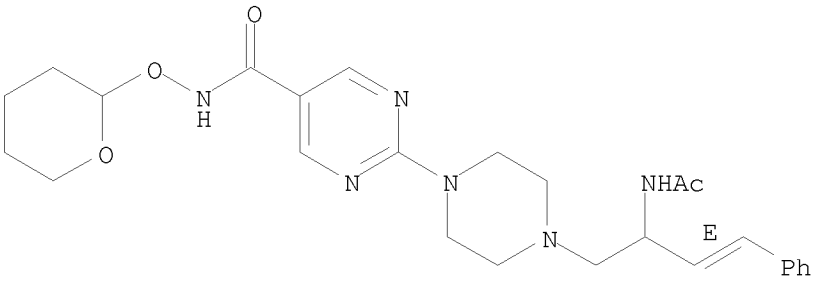
CRN 76-05-1
CMF C2 H F3 O2



IT 944739-19-9P 944739-25-7P 944739-27-9P
944739-36-0P 944739-42-8P 944739-65-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrimidine derivs. as histone deacetylase inhibitors)

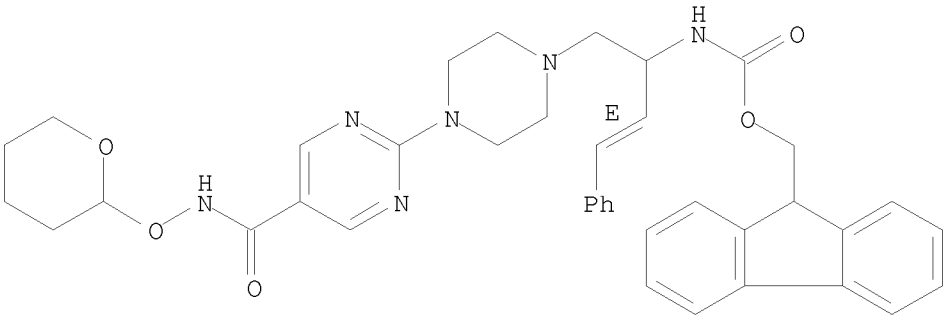
RN 944739-19-9 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-(acetylamino)-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)

Double bond geometry as shown.



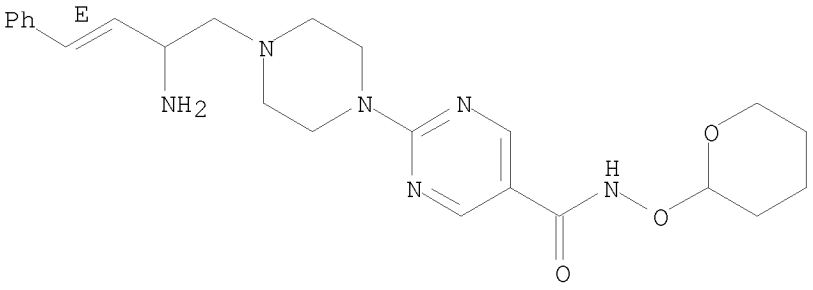
RN 944739-25-7 CAPLUS
CN Carbamic acid, N-[(2E)-3-phenyl-1-[[4-[5-[[[(tetrahydro-2H-pyran-2-yl)oxy]amino]carbonyl]-2-pyrimidinyl]-1-piperazinyl]methyl]-2-propen-1-yl]-, 9H-fluoren-9-ylmethyl ester (CA INDEX NAME)

Double bond geometry as shown.



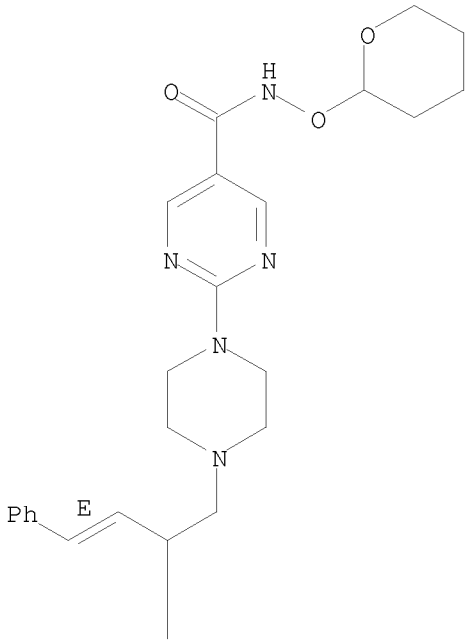
RN 944739-27-9 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-amino-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)

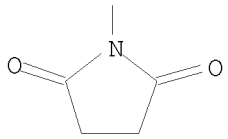
Double bond geometry as shown.



RN 944739-36-0 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-(2,5-dioxo-1-pyrrolidinyl)-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)

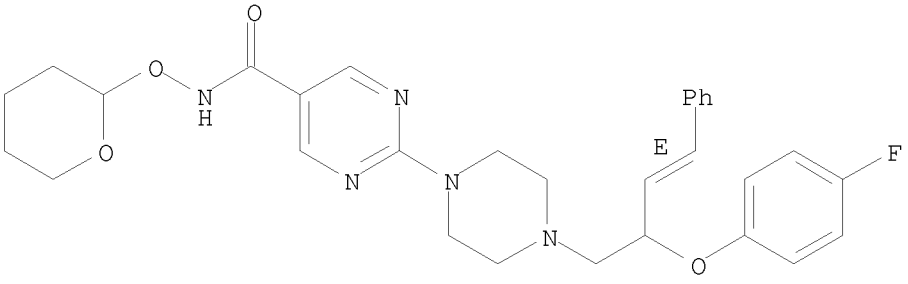
Double bond geometry as shown.





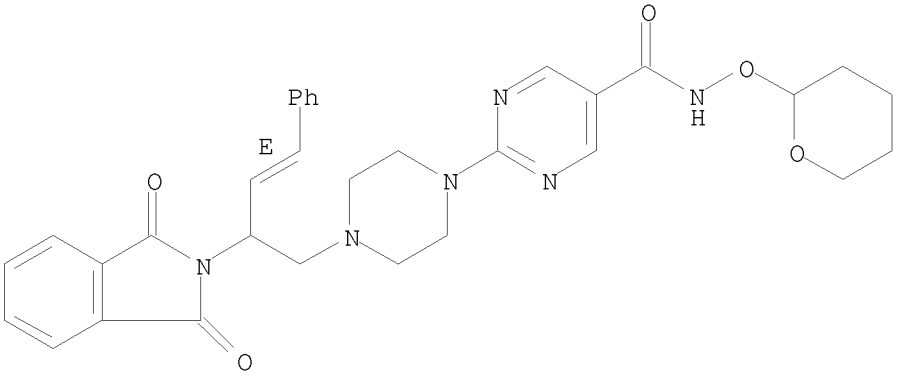
RN 944739-42-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-(4-fluorophenoxy)-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)

Double bond geometry as shown.



RN 944739-65-5 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)

Double bond geometry as shown.



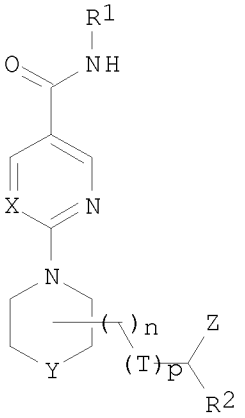
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:816806 CAPLUS
DOCUMENT NUMBER: 147:211902
TITLE: Preparation of pyrimidine derivatives as histone deacetylase inhibitors
INVENTOR(S): Angibaud, Patrick Rene; Van Brandt, Sven Franciscus Anna; Marconnet-Decrane, Laurence Francoise Bernadette; Roux, Bruno
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 63pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007082880	A1	20070726	WO 2007-EP50379	20070116

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: EP 2006-100571 A 20060119
OTHER SOURCE(S): MARPAT 147:211902
GI



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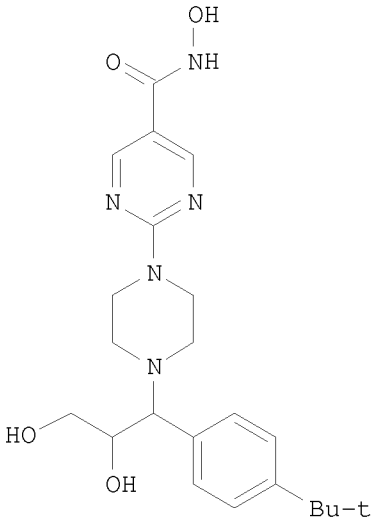


II

AB The title compds. with general formula I [wherein R1 = OH or substituted phenyl; R2 = -CH2OH, -CH2OCH3, -CH2OCH2CH3, or -CH2CH(OH)CH2OH; T = N(R3), where R3 = H, alkyl, cycloalkyl, etc.; X = N or CH; Y = O, NH, CH2, etc.; n = 0-1; p = 0-1, provided that when p = 0 then n = 0 and Y = N, and -CH(R2)-Z is attached to Y; Z = (un)substituted aryl or heteroaryl] or N-oxide forms, pharmaceutically acceptable salts, or stereoisomeric forms thereof were prepared as histone deacetylase (HDAC) inhibitors for the treatment of proliferative diseases. For example, compound II was prepared in a multi-step synthesis. In vitro assay for inhibition of HDAC was performed to measure the inhibition of HDAC enzymic activity, and colorimetric assay was performed to determine cellular activity on A2780 tumor cells. II showed HDAC inhibitory and anti-proliferative activities in the above two assays with pIC50 values of 7.0 and 7.1, resp. Formulations containing I as active ingredients were also reported.

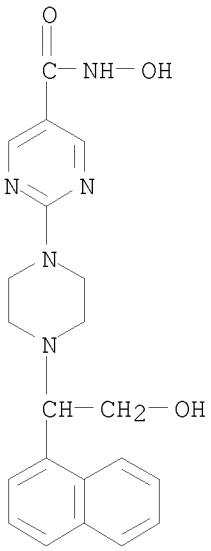
IT 944712-03-2P 944712-05-4P 944712-07-6P
944712-09-8P 944712-10-1P 944712-12-3P
944712-14-5P 944712-16-7P 944712-18-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyrimidine derivs. as histone deacetylase inhibitors)

RN 944712-03-2 CAPLUS

CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[2-hydroxy-1-(1-naphthalenyl)ethyl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

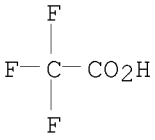
CM 1

CRN 944712-02-1
CMF C21 H23 N5 O3



CM 2

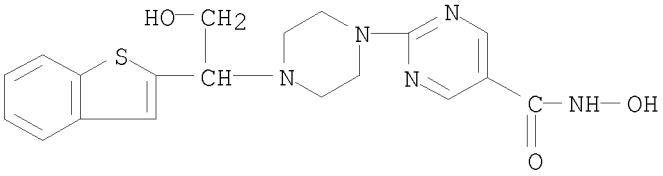
CRN 76-05-1
CMF C2 H F3 O2



RN 944712-05-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-(1-benzo[b]thien-2-yl-2-hydroxyethyl)-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

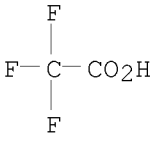
CM 1

CRN 944712-04-3
CMF C19 H21 N5 O3 S



CM 2

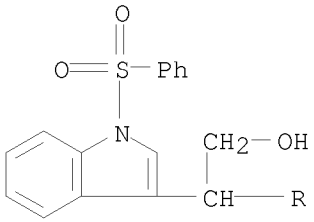
CRN 76-05-1
CMF C2 H F3 O2

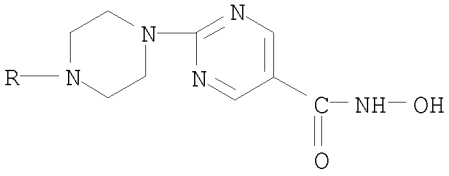


RN 944712-07-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[2-hydroxy-1-[1-(phenylsulfonyl)-1H-indol-3-yl]ethyl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

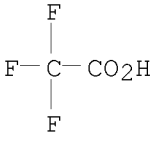
CRN 944712-06-5
CMF C25 H26 N6 O5 S





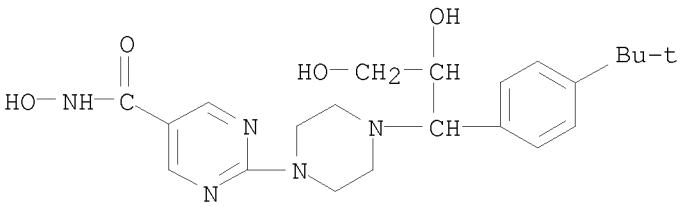
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 944712-09-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[4-(1,1-dimethylethyl)phenyl]-2,3-

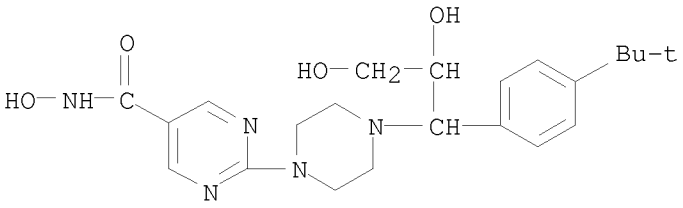
dihydroxypropyl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



RN 944712-10-1 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[4-(1,1-dimethylethyl)phenyl]-2,3-dihydroxypropyl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

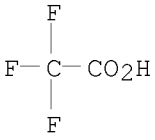
CM 1

CRN 944712-09-8
CMF C22 H31 N5 O4



CM 2

CRN 76-05-1
CMF C2 H F3 O2

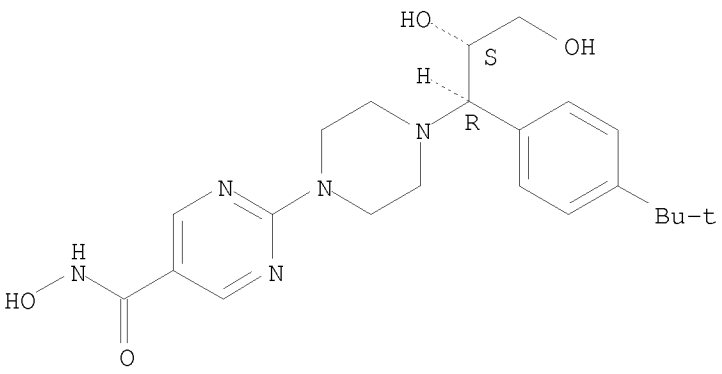


RN 944712-12-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(1R,2S)-1-[4-(1,1-dimethylethyl)phenyl]-2,3-dihydroxypropyl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

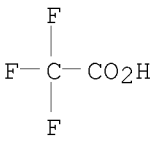
CRN 944712-11-2
CMF C22 H31 N5 O4

Absolute stereochemistry.



CM 2

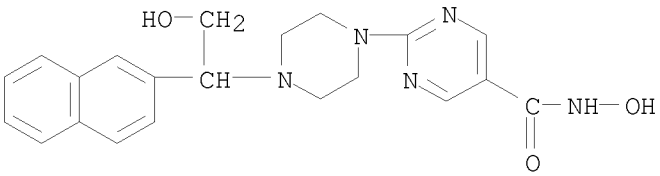
CRN 76-05-1
CMF C2 H F3 O2



RN 944712-14-5 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[2-hydroxy-1-(2-naphthalenyl)ethyl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

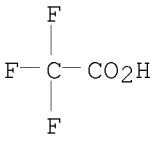
CM 1

CRN 944712-13-4
CMF C21 H23 N5 O3



CM 2

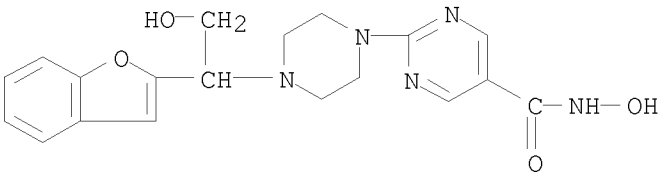
CRN 76-05-1
CMF C2 H F3 O2



RN 944712-16-7 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-(2-benzofuranyl)-2-hydroxyethyl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

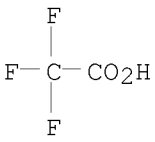
CM 1

CRN 944712-15-6
CMF C19 H21 N5 O4



CM 2

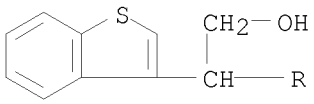
CRN 76-05-1
CMF C2 H F3 O2

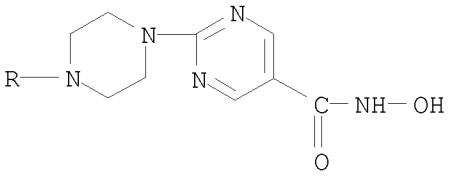


RN 944712-18-9 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-(1-benzo[b]thien-3-yl-2-hydroxyethyl)-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

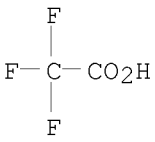
CRN 944712-17-8
CMF C19 H21 N5 O3 S





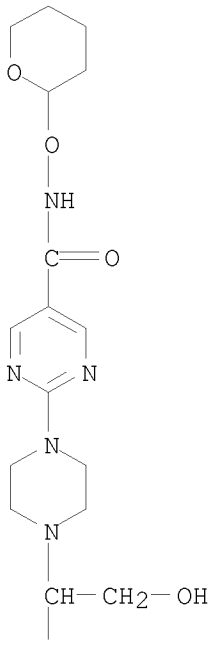
CM 2

CRN 76-05-1
CMF C2 H F3 O2

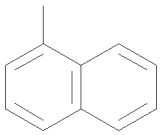


IT 944712-19-0P 944712-20-3P 944712-23-6P
944712-27-0P 944712-30-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrimidine derivs. as histone deacetylase inhibitors)
RN 944712-19-0 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[2-hydroxy-1-(1-naphthalenyl)ethyl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)

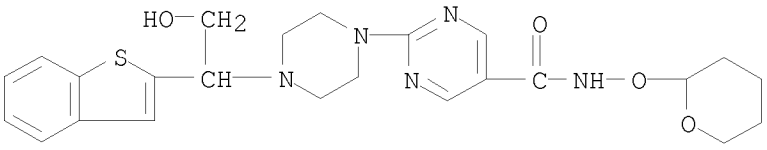
PAGE 1-A



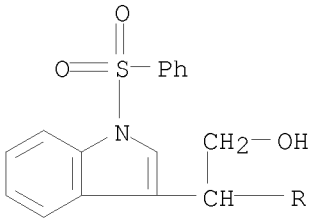
PAGE 2-A

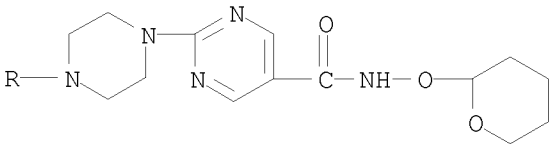


RN 944712-20-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-(1-benzo[b]thien-2-yl-2-hydroxyethyl)-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)

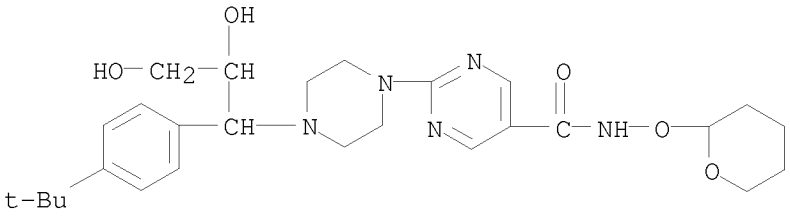


RN 944712-23-6 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[2-hydroxy-1-[1-(phenylsulfonyl)-1H-indol-3-yl]ethyl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)



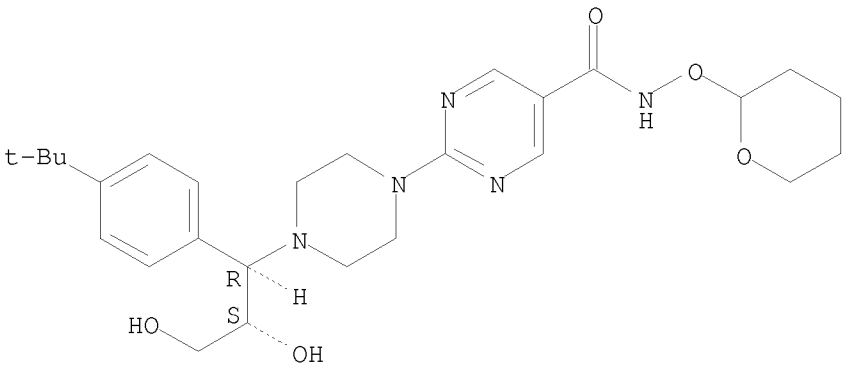


RN 944712-27-0 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[4-(1,1-dimethylethyl)phenyl]-2,3-dihydroxypropyl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)



RN 944712-30-5 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(1R,2S)-1-[4-(1,1-dimethylethyl)phenyl]-2,3-dihydroxypropyl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)

Absolute stereochemistry.

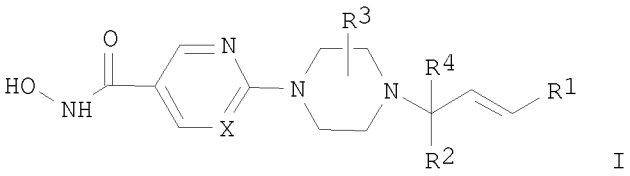


REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:101446 CAPLUS
DOCUMENT NUMBER: 144:192266
TITLE: Preparation of substituted propenyl piperazine derivatives as novel inhibitors of histone deacetylase
INVENTOR(S): Van Brandt, Sven Franciscus Anna; Van Emelen, Kristof; Angibaud, Patrick Rene; Marconnet-Decrane, Laurence Francoise Bernadette; Arts, Janine
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2006010749	A2	20060202	WO 2005-EP53611		20050725
WO 2006010749	A3	20060608			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
AU 2005266311	A1	20060202	AU 2005-266311		20050725
CA 2572971	A1	20060202	CA 2005-2572971		20050725
EP 1776358	A2	20070425	EP 2005-777776		20050725
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU					
CN 1993356	A	20070704	CN 2005-80025487		20050725
JP 2008508234	T	20080321	JP 2007-523072		20050725
BR 2005013891	A	20080520	BR 2005-13891		20050725
KR 2007043978	A	20070426	KR 2007-701641		20070123
US 20070135424	A1	20070614	US 2007-626215		20070123
IN 2007DN00658	A	20070803	IN 2007-DN658		20070124
MX 200701119	A	20070315	MX 2007-1119		20070126
NO 2007001117	A	20070227	NO 2007-1117		20070227
PRIORITY APPLN. INFO.:			EP 2004-77171	A	20040728
			US 2004-592357P	P	20040729
			WO 2005-EP53611	W	20050725

OTHER SOURCE(S): CASREACT 144:192266; MARPAT 144:192266
GI



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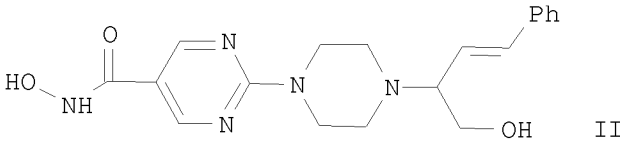

II

AB Substituted propenyl piperazine derivs. I, wherein X is independently N or CH; R1 is Ph, naphthalenyl or heterocyclyl; wherein each of said Ph or naphthalenyl is optionally substituted with one or two substituents each independently selected from halo, alkyl, alkyloxy, poly-halo-alkyl, aryl, hydroxy, cyano, amino, alkylcarbonylamino, alkylsulfonylamino, hydroxycarbonyl, alkyloxycarbonyl, hydroxyalkyl, alkyloxymethyl, aminomethyl, alkylaminomethyl, alkylcarbonylaminomethyl, alkylsulfonylaminomethyl, aminosulfonyl, alkylaminosulfonyl or heterocyclyl; R2 is hydrogen, -CH2R5, trifluoromethyl, -C(O)-R6, or -CH-NR7R8; wherein each R5 is independently hydrogen, hydroxy, alkyloxy, alkyloxyalkyloxy, alkylcarbonyloxy, piperazinyl, N-methylpiperazinyl, morpholinyl, thiomorpholinyl, imidazolyl or triazolyl; each R6 is independently hydroxy, alkyloxy, amino or mono- or di(alkyl)amino, cycloalkylamino, hydroxyalkylamino, piperazinyl, N-methylpiperazinyl, morpholinyl or thiomorpholinyl; each R7 and R8 are independently hydrogen, alkyl, alkylcarbonyl, alkylsulfonyl, or mono- or di(alkyl)aminosulfonyl; R3 is hydrogen, hydroxymethyl, aminomethyl or mono- or di(alkyl)aminomethyl; R4 is hydrogen or alkyl; were prepared and having histone deacetylase inhibiting enzymic activity and to inhibit proliferative conditions, such as cancer and psoriasis. Thus, propenyl piperazine derivative II was prepared and tested in vitro and in nude mice as inhibitor of histone deacetylase and was better than R306465 after oral administration. P21 enzyme linked immunosorbent assay has been applied to determine the p21 protein expression level in human A2780 ovarian carcinoma cells. In vitro assay for inhibition of histone deacetylase is reported. P21 induction was measured as the consequence of DNA damage or as the consequence of histone deacetylase inhibition. Antiproliferative activity of title compds. was determined on A2780 cells (neg. log value of the IC50, pIC50 = 7.9-8.2).

IT 875138-85-5P 875138-87-7P 875138-88-8P
875138-89-9P 875138-90-2P 875138-91-3P
875138-93-5P 875138-94-6P 875138-98-0P
875139-00-7P 875139-02-9P 875139-04-1P
875139-06-3P 875139-07-4P 875139-09-6P
875139-11-0P 875139-13-2P 875139-14-3P
875139-15-4P 875139-17-6P 875139-19-8P
875139-20-1P 875139-21-2P 875139-23-4P
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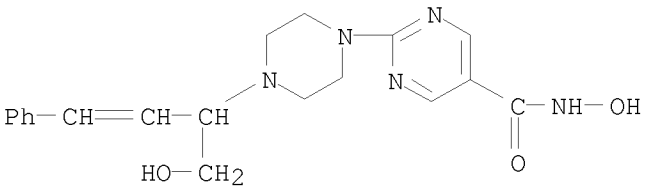
875139-27-8P 875139-28-9P 875139-29-0P
875139-30-3P 875139-31-4P 875139-69-8P

875139-70-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted propenyl piperazine derivs. as novel inhibitors of histone deacetylase)

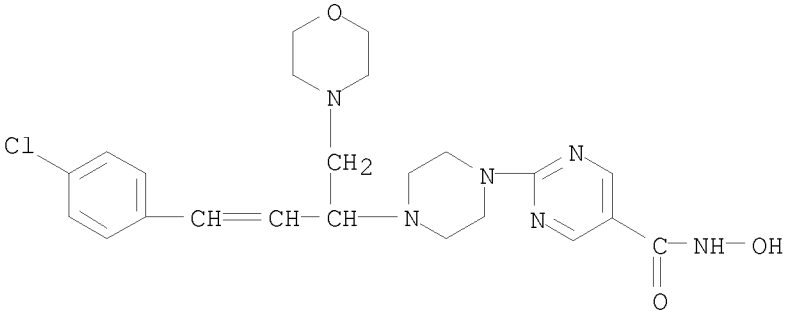
RN 875138-85-5 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(hydroxymethyl)-3-phenyl-2-propen-1-yl]-1-piperazinyl]- (CA INDEX NAME)



RN 875138-87-7 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3-(4-chlorophenyl)-1-(4-morpholinylmethyl)-2-propen-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

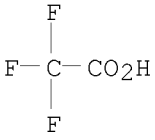
CM 1

CRN 875138-86-6
CMF C23 H29 Cl N6 O3



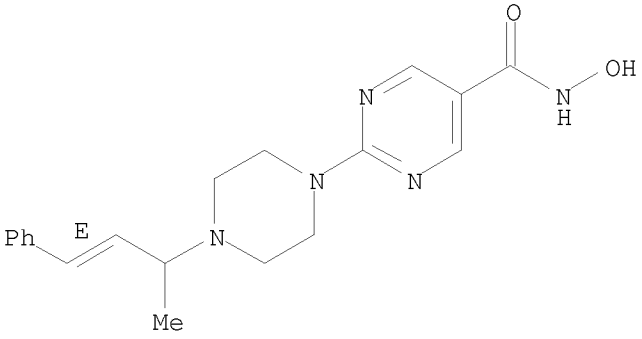
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 875138-88-8 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(2E)-1-methyl-3-phenyl-2-propen-1-yl]-1-piperazinyl]- (CA INDEX NAME)

Double bond geometry as shown.

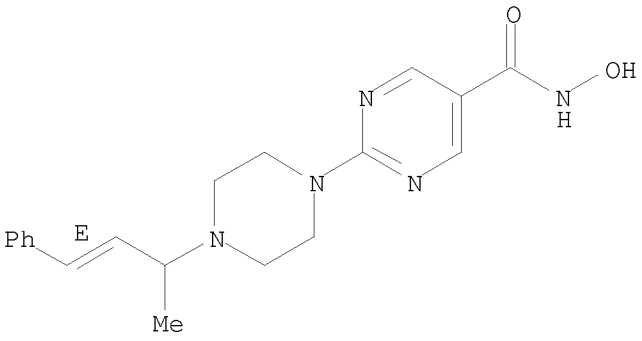


RN 875138-89-9 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(2E)-1-methyl-3-phenyl-2-propen-1-yl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

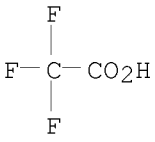
CRN 875138-88-8
CMF C19 H23 N5 O2

Double bond geometry as shown.

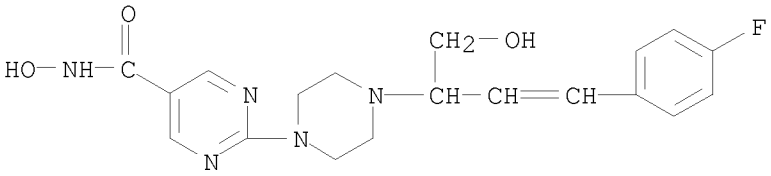


CM 2

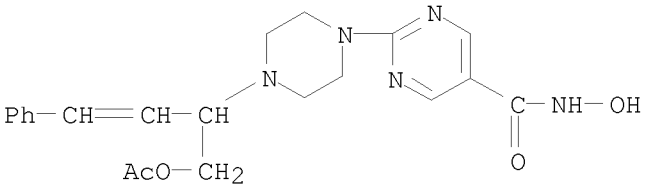
CRN 76-05-1
CMF C2 H F3 O2



RN 875138-90-2 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3-(4-fluorophenyl)-1-(hydroxymethyl)-2-propen-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



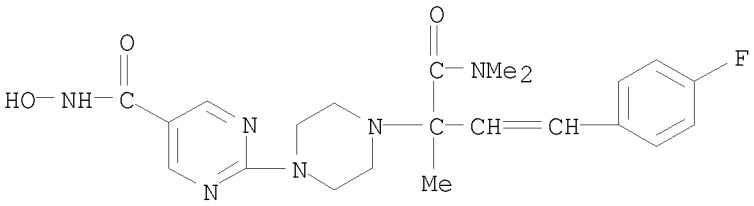
RN 875138-91-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[(acetyloxy)methyl]-3-phenyl-2-propen-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



RN 875138-93-5 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[(dimethylamino)carbonyl]-3-(4-fluorophenyl)-1-methyl-2-propen-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

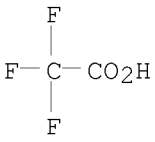
CM 1

CRN 875138-92-4
CMF C22 H27 F N6 O3

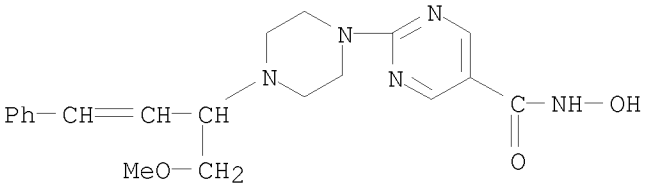


CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 875138-94-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(methoxymethyl)-3-phenyl-2-propen-1-yl]-1-piperazinyl]- (CA INDEX NAME)

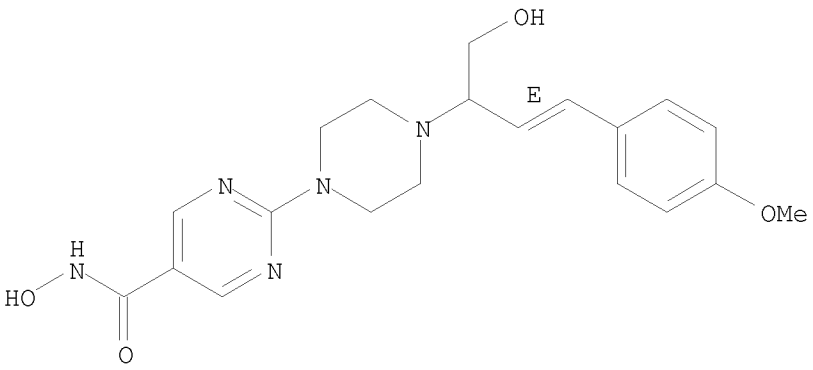


RN 875138-98-0 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(2E)-1-(hydroxymethyl)-3-(4-methoxyphenyl)-2-propen-1-yl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 875138-97-9
CMF C20 H25 N5 O4

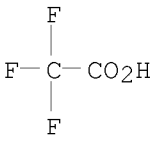
Double bond geometry as shown.



CM 2

CRN 76-05-1

CMF C2 H F3 O2

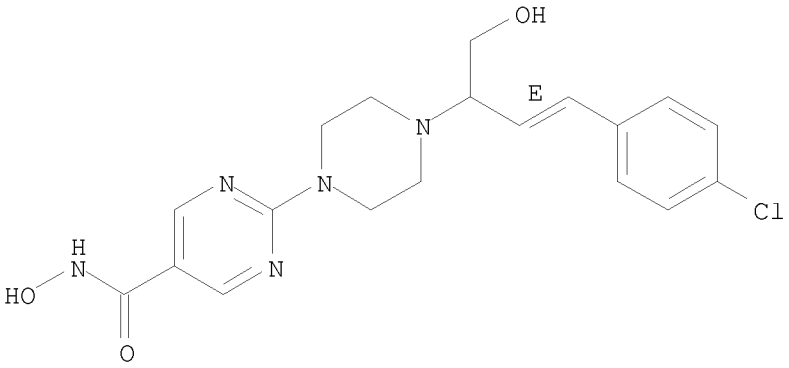


RN 875139-00-7 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(2E)-3-(4-chlorophenyl)-1-(hydroxymethyl)-2-propen-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 875138-99-1
CMF C19 H22 Cl N5 O3

Double bond geometry as shown.



CM 2

CRN 76-05-1
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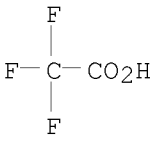
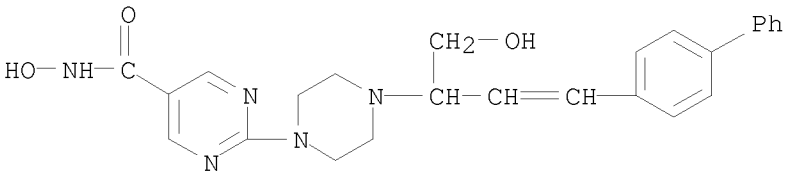


RN 875139-02-9 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3-[1,1'-biphenyl]-4-yl-1-(hydroxymethyl)-2-propen-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 875139-01-8
CMF C25 H27 N5 O3



CM 2

CRN 76-05-1
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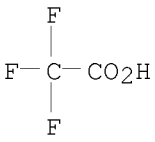
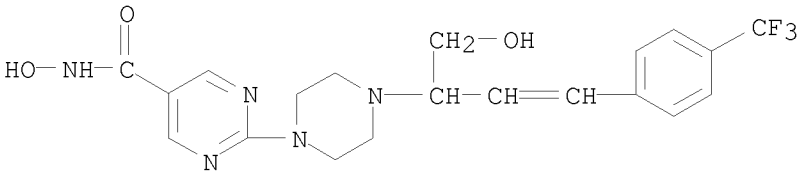


RN 875139-04-1 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(hydroxymethyl)-3-[4-(trifluoromethyl)phenyl]-2-propen-1-yl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

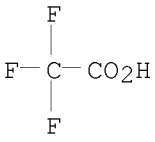
CM 1

CRN 875139-03-0
CMF C20 H22 F3 N5 O3



CM 2

CRN 76-05-1
CMF C2 H F3 O2

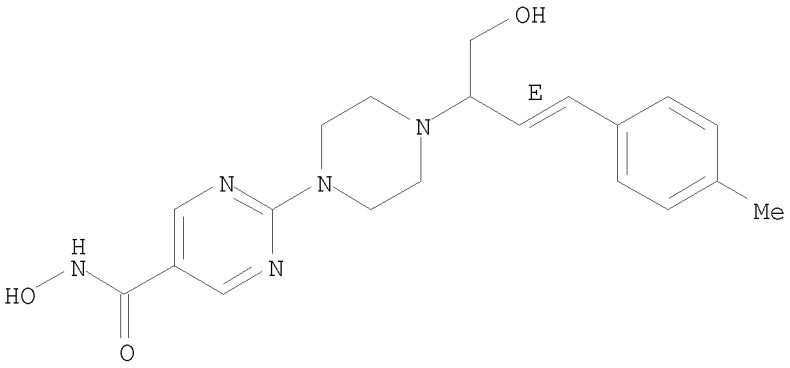


RN 875139-06-3 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(2E)-1-(hydroxymethyl)-3-(4-methylphenyl)-2-propen-1-yl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

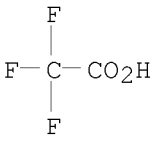
CRN 875139-05-2
CMF C20 H25 N5 O3

Double bond geometry as shown.

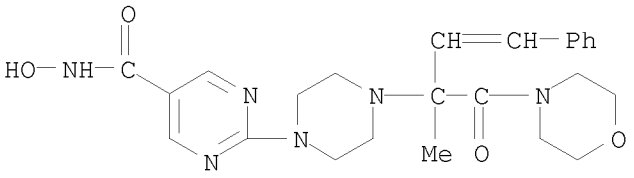


CM 2

CRN 76-05-1
CMF C2 H F3 O2



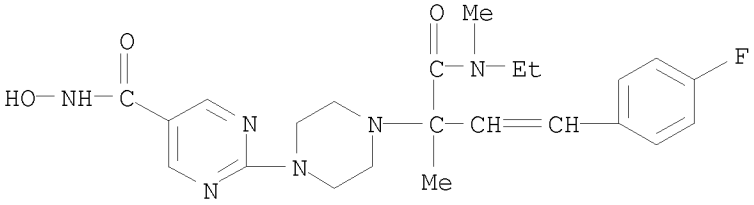
RN 875139-07-4 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-methyl-1-(4-morpholinylcarbonyl)-3-phenyl-2-propen-1-yl]-1-piperazinyl]- (CA INDEX NAME)



RN 875139-09-6 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[(ethylmethylamino)carbonyl]-3-(4-fluorophenyl)-1-methyl-2-propen-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

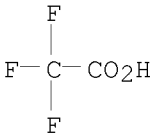
CM 1

CRN 875139-08-5
CMF C23 H29 F N6 O3



CM 2

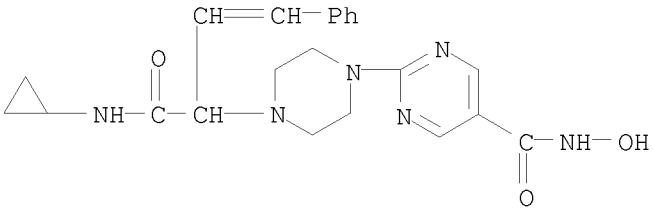
CRN 76-05-1
CMF C2 H F3 O2



RN 875139-11-0 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[(cyclopropylamino)carbonyl]-3-phenyl-2-propen-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

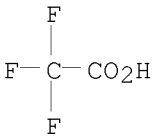
CM 1

CRN 875139-10-9
CMF C22 H26 N6 O3



CM 2

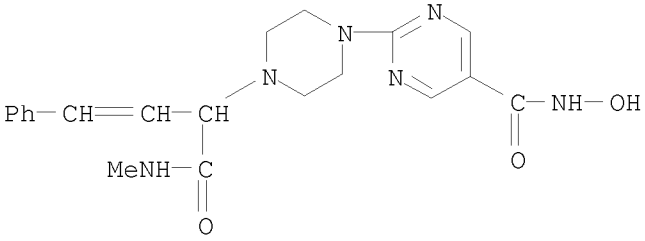
CRN 76-05-1
CMF C2 H F3 O2



RN 875139-13-2 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-[(methylamino)carbonyl]-3-phenyl-2-propen-1-yl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

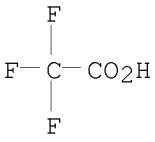
CM 1

CRN 875139-12-1
CMF C20 H24 N6 O3

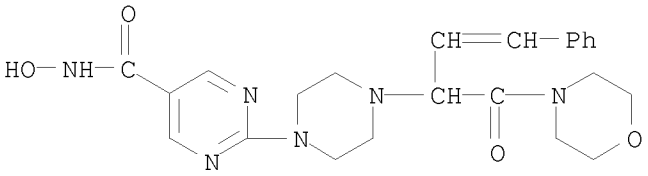


CM 2

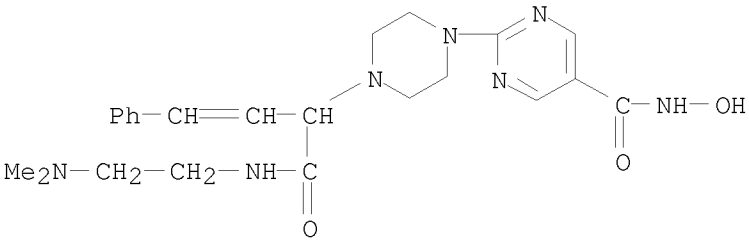
CRN 76-05-1
CMF C2 H F3 O2



RN 875139-14-3 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(4-morpholinylcarbonyl)-3-phenyl-2-propen-1-yl]-1-piperazinyl]- (CA INDEX NAME)



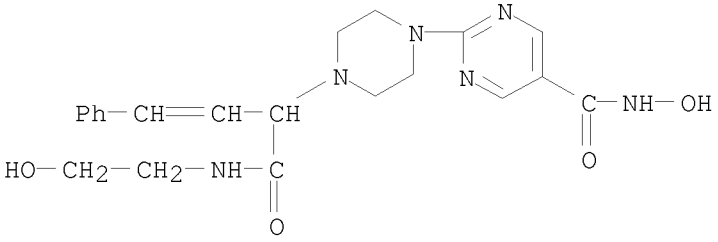
RN 875139-15-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[[[2-(dimethylamino)ethyl]amino]carbonyl]-3-phenyl-2-propen-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



RN 875139-17-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-[[(2-hydroxyethyl)amino]carbonyl]-3-phenyl-2-propen-1-yl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

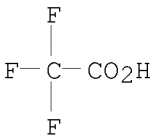
CM 1

CRN 875139-16-5
CMF C21 H26 N6 O4



CM 2

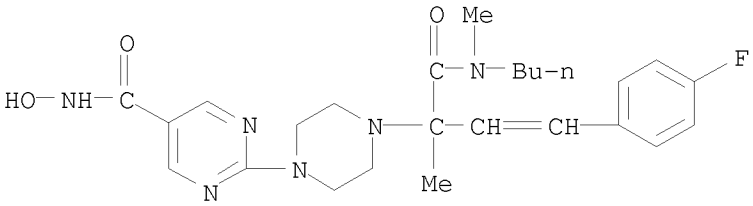
CRN 76-05-1
CMF C2 H F3 O2



RN 875139-19-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[(butylmethylamino)carbonyl]-3-(4-fluorophenyl)-1-methyl-2-propen-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

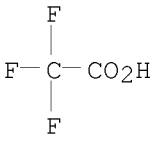
CM 1

CRN 875139-18-7
CMF C25 H33 F N6 O3

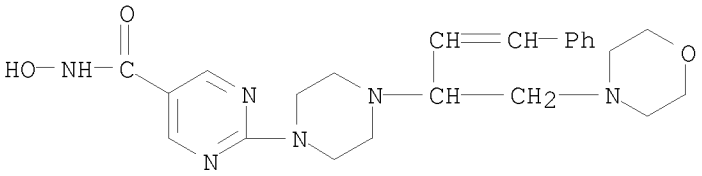


CM 2

CRN 76-05-1
CMF C2 H F3 O2

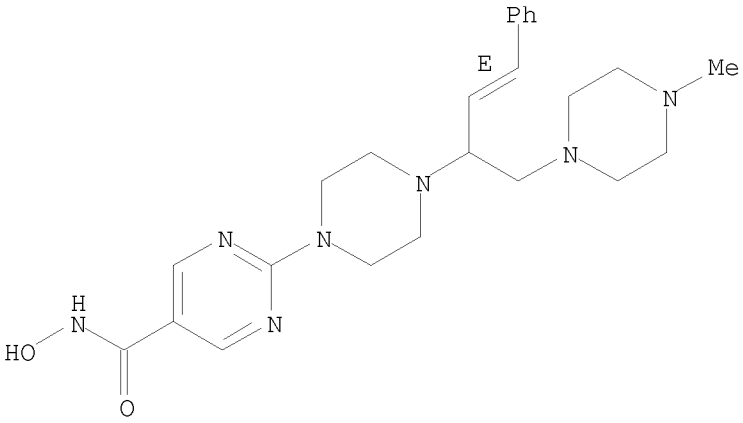


RN 875139-20-1 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(4-morpholinylmethyl)-3-phenyl-2-propen-1-yl]-1-piperazinyl]- (CA INDEX NAME)



RN 875139-21-2 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(2E)-1-[(4-methyl-1-piperazinyl)methyl]-3-phenyl-2-propen-1-yl]-1-piperazinyl]- (CA INDEX NAME)

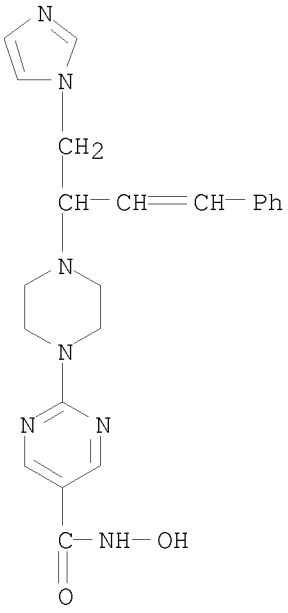
Double bond geometry as shown.



RN 875139-23-4 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(1H-imidazol-1-ylmethyl)-3-phenyl-2-propen-1-yl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

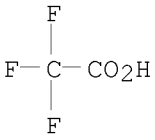
CM 1

CRN 875139-22-3
CMF C22 H25 N7 O2

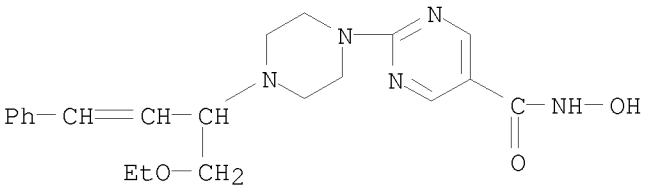


CM 2

CRN 76-05-1
CMF C2 H F3 O2



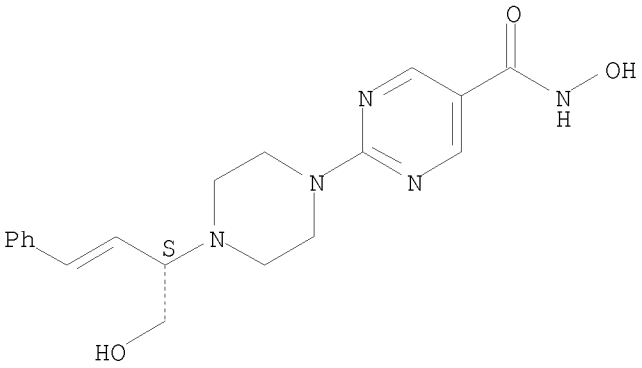
RN 875139-24-5 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-(ethoxymethyl)-3-phenyl-2-propen-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



RN 875139-25-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(1S)-1-(hydroxymethyl)-3-phenyl-2-propen-1-yl]-1-piperazinyl]- (CA INDEX NAME)

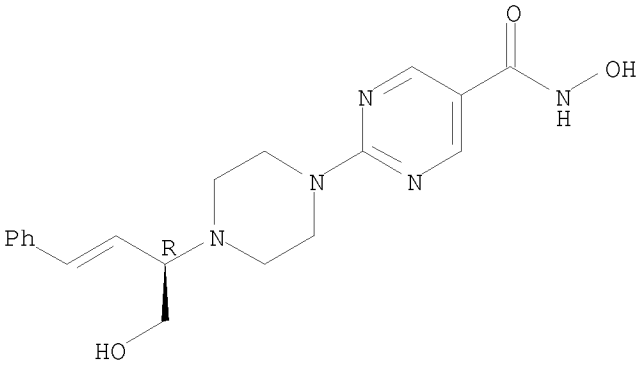
Absolute stereochemistry.

Double bond geometry unknown.



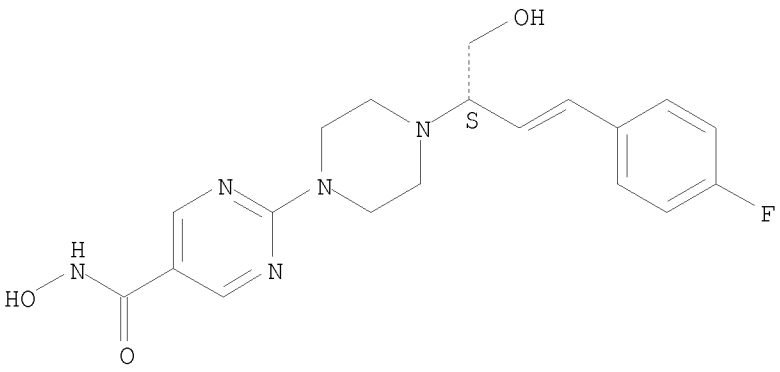
RN 875139-26-7 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(1R)-1-(hydroxymethyl)-3-phenyl-2-propen-1-yl]-1-piperazinyl]- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

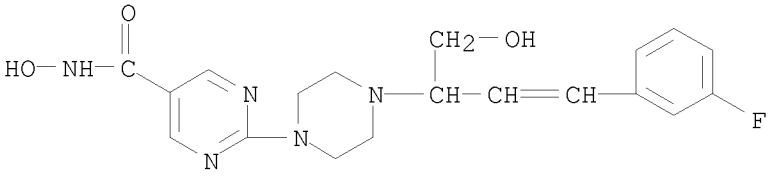


RN 875139-27-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(1S)-3-(4-fluorophenyl)-1-(hydroxymethyl)-2-propen-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)

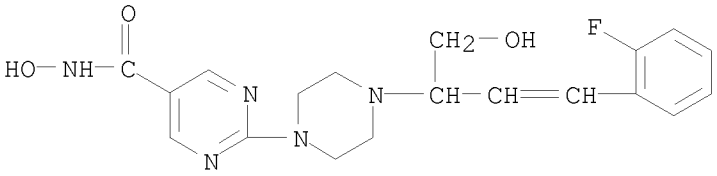
Absolute stereochemistry.
Double bond geometry unknown.



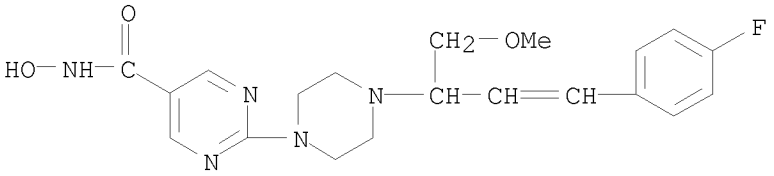
RN 875139-28-9 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3-(3-fluorophenyl)-1-(hydroxymethyl)-2-propen-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



RN 875139-29-0 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3-(2-fluorophenyl)-1-(hydroxymethyl)-2-propen-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



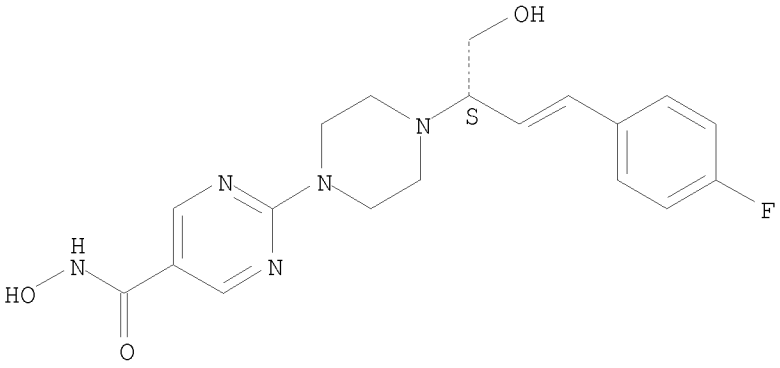
RN 875139-30-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3-(4-fluorophenyl)-1-(methoxymethyl)-2-propen-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



RN 875139-31-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(1S)-3-(4-fluorophenyl)-1-(hydroxymethyl)-2-

propen-1-yl]-1-piperazinyl]-N-hydroxy-, hydrochloride (1:1) (CA INDEX NAME)

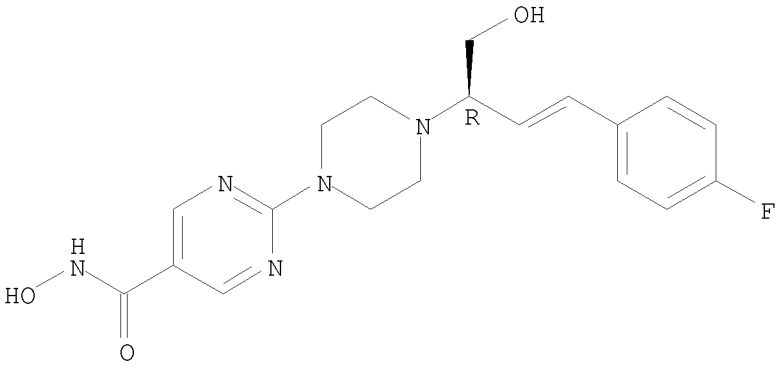
Absolute stereochemistry.
Double bond geometry unknown.



● HCl

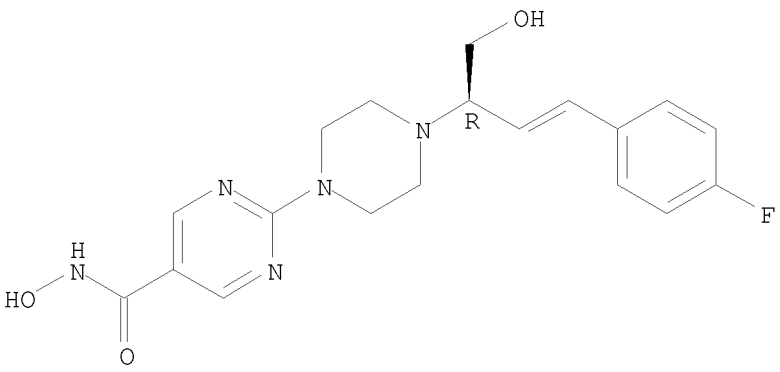
RN 875139-69-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(1R)-3-(4-fluorophenyl)-1-(hydroxymethyl)-2-propen-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 875139-70-1 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(1R)-3-(4-fluorophenyl)-1-(hydroxymethyl)-2-propen-1-yl]-1-piperazinyl]-N-hydroxy-, hydrochloride (1:1) (CA INDEX NAME)

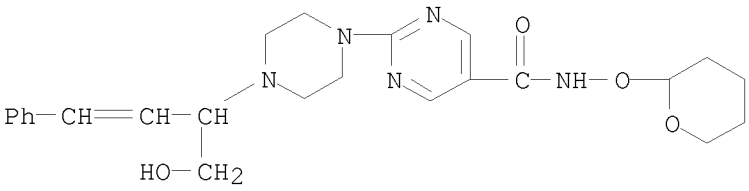
Absolute stereochemistry.
Double bond geometry unknown.



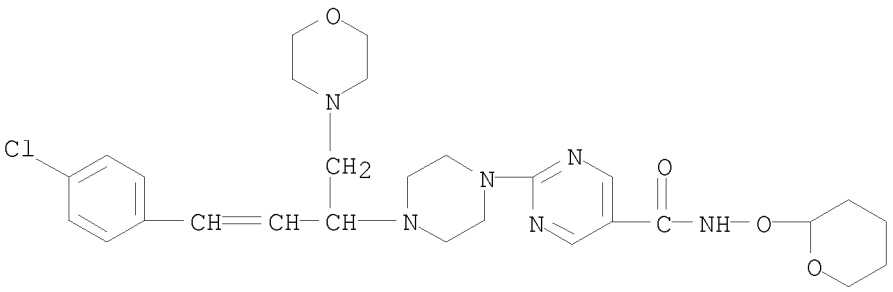
● HCl

IT 875138-54-8P 875138-59-3P 875138-62-8P
875138-66-2P 875138-70-8P 875138-73-1P
875138-77-5P 875138-78-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted propenyl piperazine derivs. as novel inhibitors of histone deacetylase)

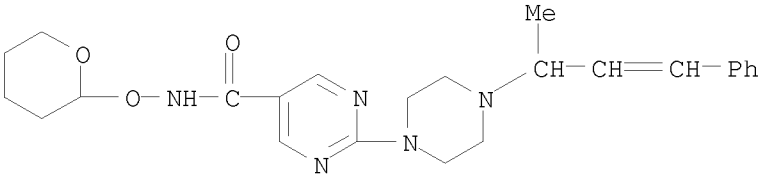
RN 875138-54-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-(hydroxymethyl)-3-phenyl-2-propen-1-yl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)



RN 875138-59-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3-(4-chlorophenyl)-1-(4-morpholinylmethyl)-2-propen-1-yl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)



RN 875138-62-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-(1-methyl-3-phenyl-2-propen-1-yl)-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)



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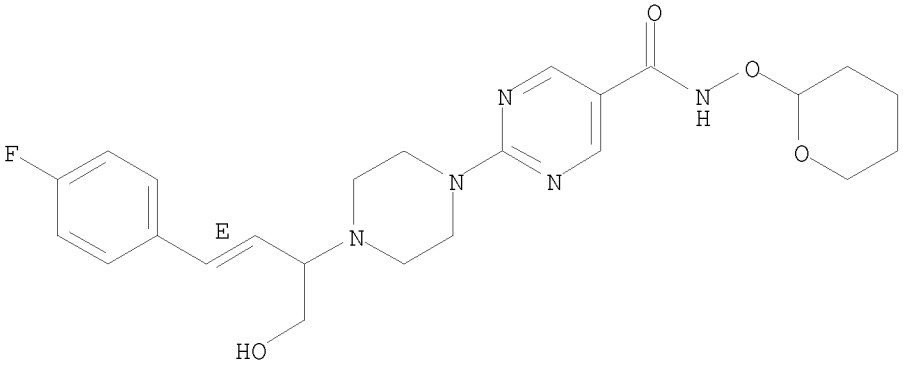
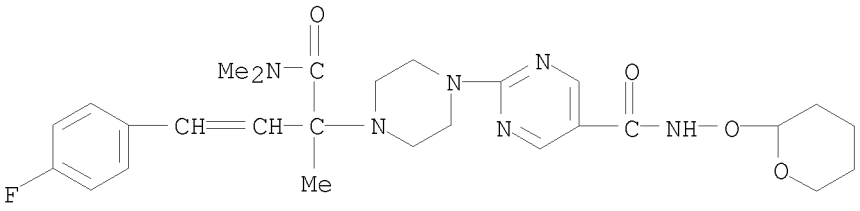
CN 5-Pyrimidinecarboxamide, 2-[4-[(2E)-3-(4-fluorophenyl)-1-(hydroxymethyl)-2-propen-1-yl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)

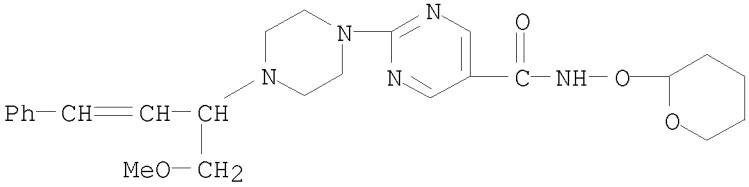
Double bond geometry as shown.



RN 875138-70-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[(dimethylamino)carbonyl]-3-(4-fluorophenyl)-1-methyl-2-propen-1-yl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)



RN 875138-73-1 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-(methoxymethyl)-3-phenyl-2-propen-1-yl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)



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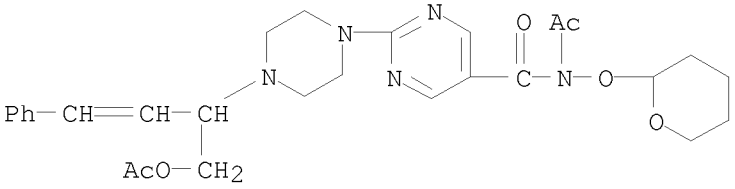
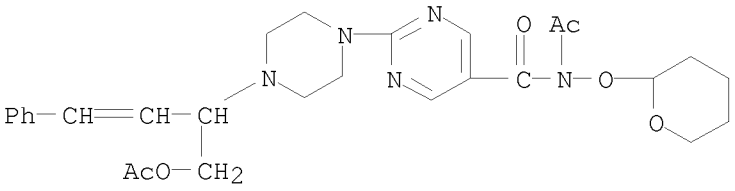
CN 5-Pyrimidinecarboxamide, N-acetyl-2-[4-[1-[(acetyloxy)methyl]-3-phenyl-2-propen-1-yl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)



RN 875138-78-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-acetyl-2-[4-[1-[(acetyloxy)methyl]-3-phenyl-2-propen-1-yl]-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]-, ethanedioate (1:1) (CA INDEX NAME)

CM 1

CRN 875138-77-5
CMF C28 H35 N5 O6



CM 2

CRN 144-62-7
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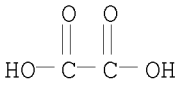

L3 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:300395 CAPLUS
DOCUMENT NUMBER: 142:355054
TITLE: Preparation of amide derivatives as inhibitors of histone deacetylase
INVENTOR(S): Moradei, Oscar; Paquin, Isabelle; Leit, Silvana; Frechette, Sylvie; Vaisburg, Arkadii; Besterman, Jeffrey M.; Tessier, Pierre; Mallais, Tammy C.
PATENT ASSIGNEE(S): Methylgene, Inc., Can.
SOURCE: PCT Int. Appl., 559 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2005030705	A1	20050407	WO 2004-US31591		20040924
WO 2005030705	A9	20060420			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2004276337	A1	20050407	AU 2004-276337		20040924
CA 2539117	A1	20050407	CA 2004-2539117		20040924
EP 1663953	A1	20060607	EP 2004-789074		20040924
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CN 1882529	A	20061220	CN 2004-80034571		20040924
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PRIORITY APPLN. INFO.:			US 2003-505884P	P	20030924
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			US 2004-561082P	P	20040409
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OTHER SOURCE(S): CASREACT 142:355054; MARPAT 142:355054
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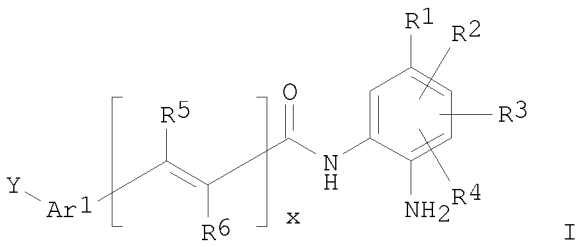

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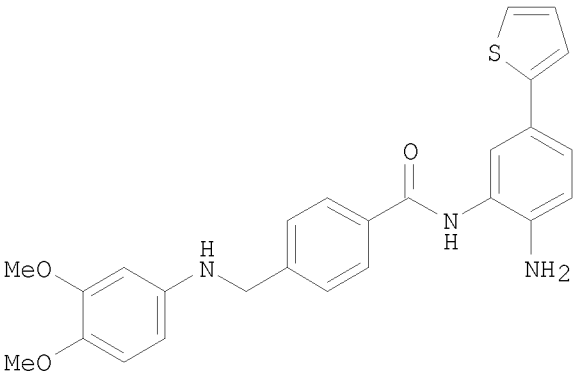

II

AB Title compds. I [Ar1 = (un)saturated-, (un)substituted-mono or fused poly-cyclic hydrocarbyl optionally containing 1-4 heteroatoms per ring; R1 = (un)substituted-mono-, -bi-, -tri-cyclic-aryl or -heteroaryl; R2, R3, and R4 independently = H, halo, amino, etc.; R5 and R6 independently = H, alkyl, aryl, etc.; x = 0-1; Y = any pharmaceutically acceptable chemical moiety consisting of 1 to 50 atoms with provisions] and their pharmaceutically acceptable salts, are prepared and disclosed as inhibitors of histone deacetylase. Thus, e.g., II was prepared by Suzuki coupling of 2-bromo-2-nitro-phenylamine (preparation given) with 2-thiopheneboronic acid followed by carbonylation with 4-[3,4-dimethoxy-(phenylamino)-methyl]benzoic acid (preparation given) and subsequent reduction The inhibitory capability of I towards antiproliferative activity of histone deacetylase enzyme was evaluated using 3-[4,5-dimethylthiazol-2-yl-2,5-diphenyltetrazolium] bromide (MTT) assay and it revealed that certain compds. of the invention had MTT IC 50 values in the range of below 1 up to 20 μM. I as histone deacetylase inhibitors should prove useful in the treatment of diseases such as, but not limited to, cell proliferative disease, protozoal disease, and fungal disease.

IT 603985-86-0P 603985-88-2P 603985-90-6P
603985-94-0P 603991-95-3P 603991-96-4P
603992-24-1P 603992-25-2P 603992-26-3P
603992-27-4P 603992-28-5P 604784-81-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amide derivs. as inhibitors of histone deacetylase)

RN 603985-86-0 CAPLUS

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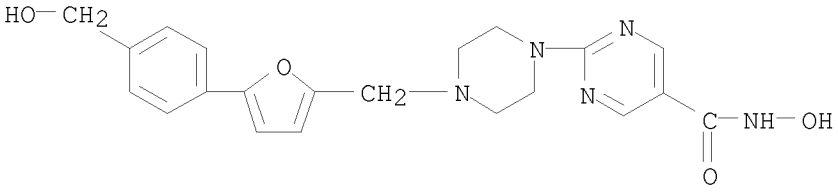

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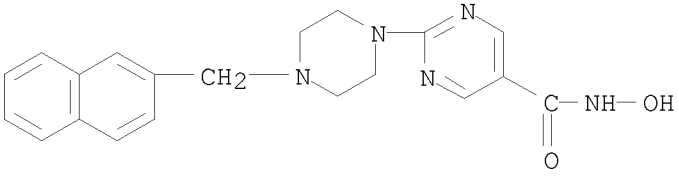

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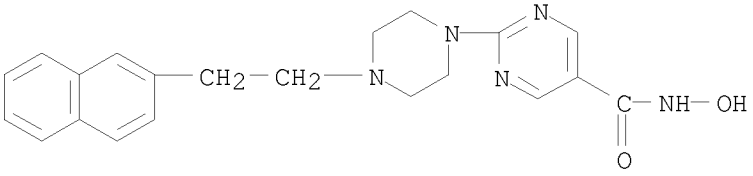

RN 603985-94-0 CAPLUS
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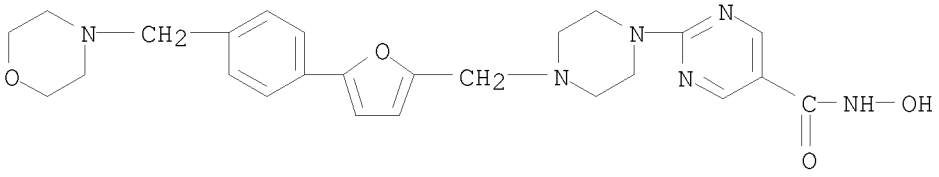

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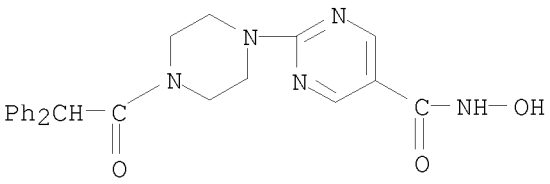

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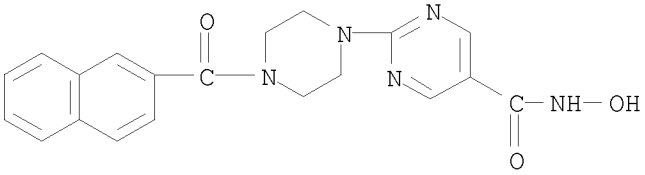

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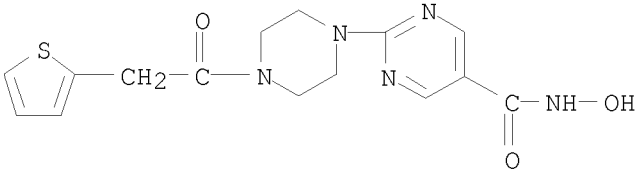

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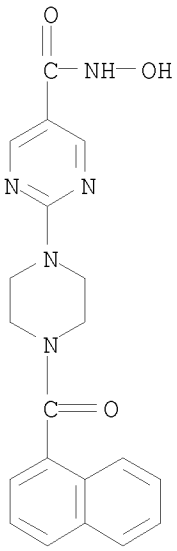

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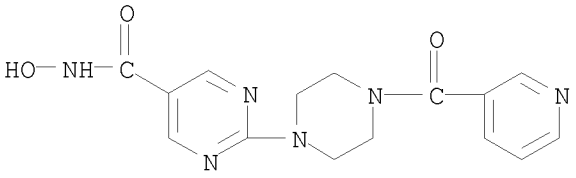

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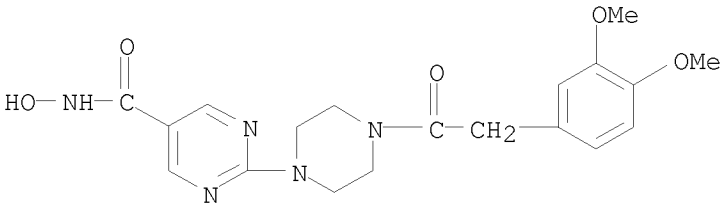

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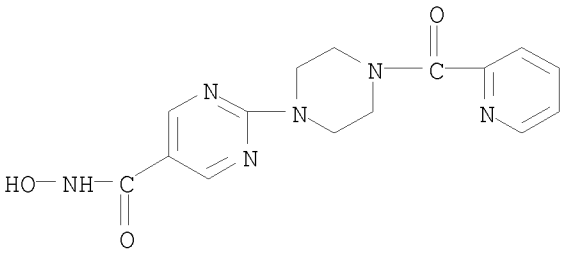

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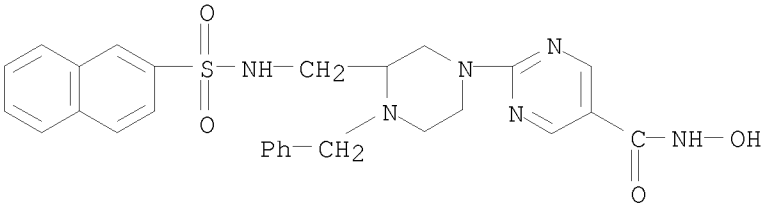

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:300394 CAPLUS
DOCUMENT NUMBER: 142:373563
TITLE: Preparation of amide derivatives as inhibitors of histone deacetylase
INVENTOR(S): Moradei, Oscar; Paquin, Isabelle; Leit, Silvana; Frechette, Sylvie; Vaisburg, Arkadii; Besterman, Jeffrey M.; Tessier, Pierre; Mallais, Tammy C.
PATENT ASSIGNEE(S): Methylgene, Inc., Can.
SOURCE: PCT Int. Appl., 389 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
JP 2008094847	A	20080424	JP 2007-281356		20071030
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			US 2003-532973P	P	20031229
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OTHER SOURCE(S): CASREACT 142:373563; MARPAT 142:373563
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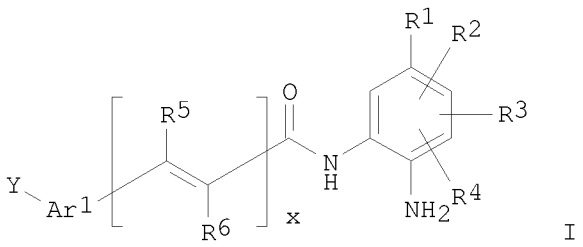

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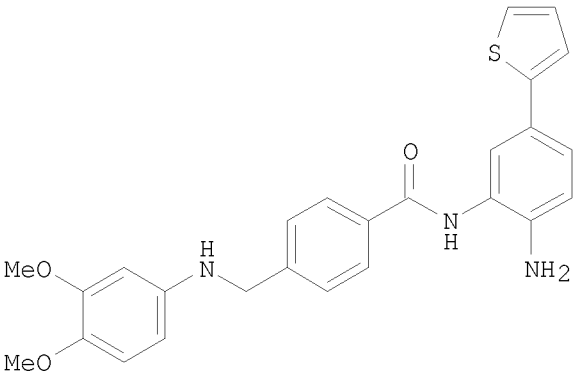

II

AB Title compds. I [Ar1 = (un)saturated-, (un)substituted-mono or fused poly-cyclic hydrocarbyl optionally containing 1-4 heteroatoms per ring; R1 = (un)substituted-mono-, -bi-, -tri-cyclic-aryl or -heteroaryl; R2, R3, and R4 independently = H, halo, amino, etc.; R5 and R6 independently = H, alkyl, aryl, etc.; x = 0-1; Y = any pharmaceutically acceptable chemical moiety consisting of 1 to 50 atoms with provisions] and their pharmaceutically acceptable salts, are prepared and disclosed as inhibitors of histone deacetylase. Thus, e.g., II was prepared by Suzuki coupling of 2-bromo-2-nitro-phenylamine (preparation given) with 2-thiopheneboronic acid followed by carbonylation with 4-[3,4-dimethoxy-(phenylamino)-methyl]benzoic acid (preparation given) and subsequent reduction The inhibitory capability of I towards antiproliferative activity of histone deacetylase enzyme was evaluated using 3-[4,5-dimethylthiazol-2-yl-2,5-diphenyltetrazolium] bromide (MTT) assay and it revealed that certain compds. of the invention had MTT IC 50 values in the range of below 1 up to 20 μM. I as histone deacetylase inhibitors should prove useful in the treatment of diseases such as, but not limited to, cell proliferative disease, protozoal disease, and fungal disease.

IT 603985-86-0P 603985-88-2P 603985-90-6P
603985-94-0P 603991-95-3P 603991-96-4P
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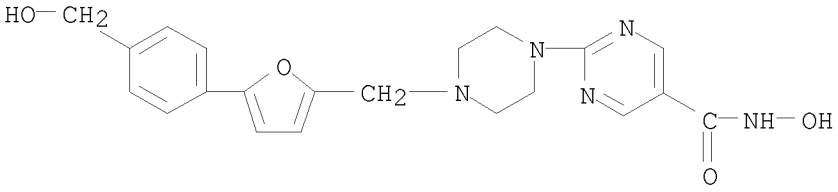
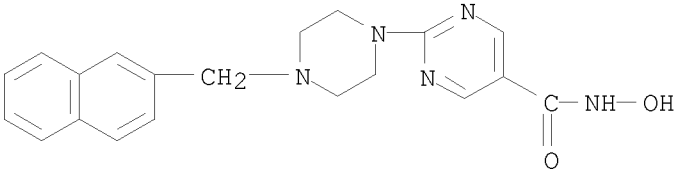


RN 603985-88-2 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-naphthalenylmethyl)-1-piperazinyl]- (CA INDEX NAME)



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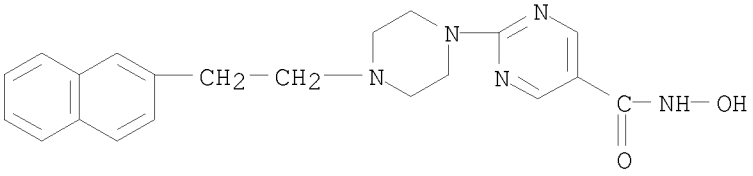

RN 603985-94-0 CAPLUS
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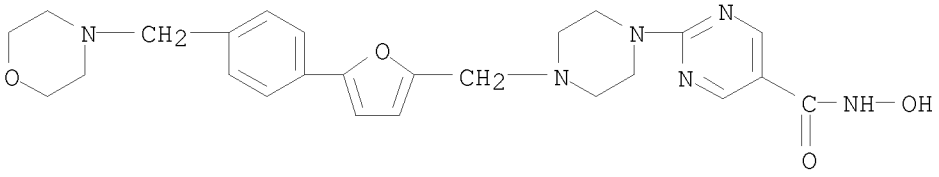

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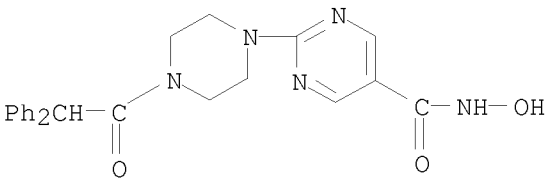

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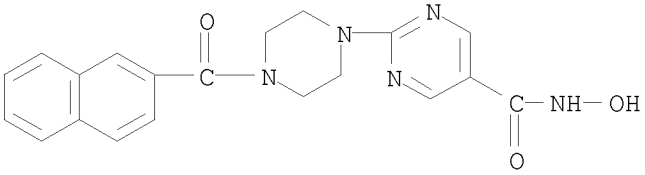

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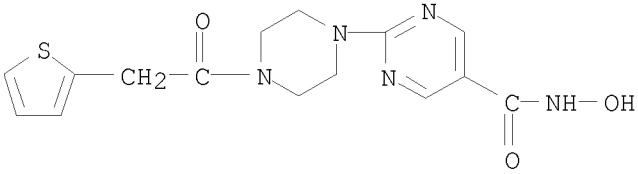

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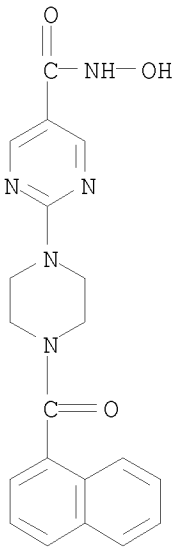

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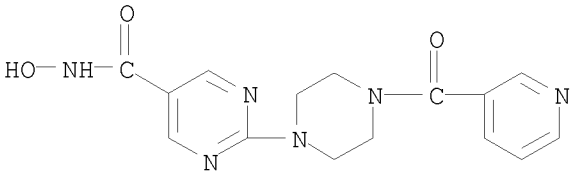

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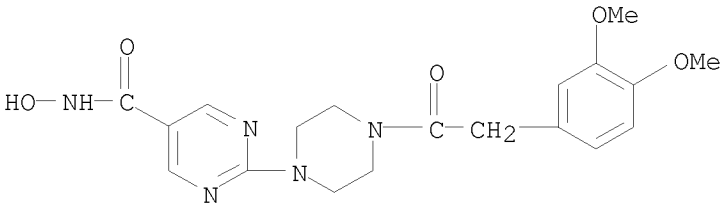

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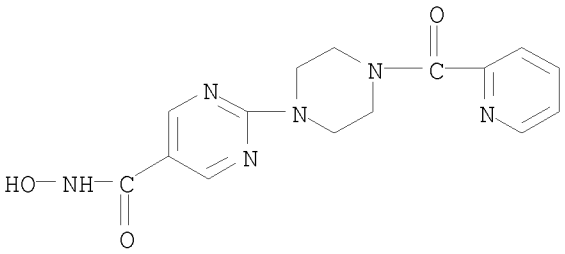
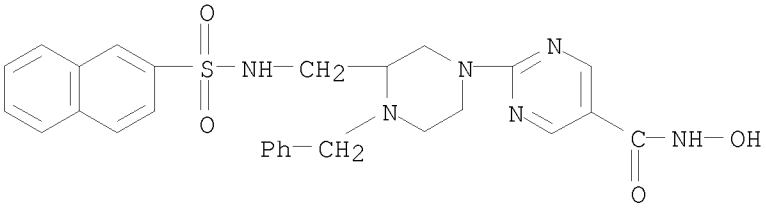


RN 604784-81-8 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[3-[[(2-naphthalenylsulfonyl)amino]methyl]-4-(phenylmethyl)-1-piperazinyl]- (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:737757 CAPLUS
DOCUMENT NUMBER: 139:276911
TITLE: Preparation of N-(piperazinylmethyl-, piperidinylmethyl- and morpholinylmethyl) sulfonamides and amides as novel inhibitors of histone deacetylase
INVENTOR(S): Van Emelen, Kristof
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076438	A1	20030918	WO 2003-EP2510	20030311
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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AU 2003218735	A1	20030922	AU 2003-218735	20030311
EP 1485378	A1	20041215	EP 2003-711979	20030311
EP 1485378	B1	20080618		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003007606	A	20041221	BR 2003-7606	20030311
CN 1642948	A	20050720	CN 2003-805921	20030311
JP 2005526766	T	20050908	JP 2003-574655	20030311
NZ 534833	A	20060728	NZ 2003-534833	20030311
CN 101007803	A	20070801	CN 2007-10005212	20030311
AT 398615	T	20080715	AT 2003-711979	20030311
TW 283676	B	20070711	TW 2003-92105285	20030312
IN 2004DN02536	A	20070413	IN 2004-DN2536	20040831
US 20050165016	A1	20050728	US 2004-507084	20040908
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PRIORITY APPLN. INFO.:	US 2002-363799P	P	20020313
	WO 2002-EP14833	A	20021223
	CN 2003-805921	A3	20030311
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OTHER SOURCE(S): MARPAT 139:276911
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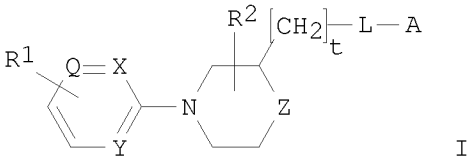

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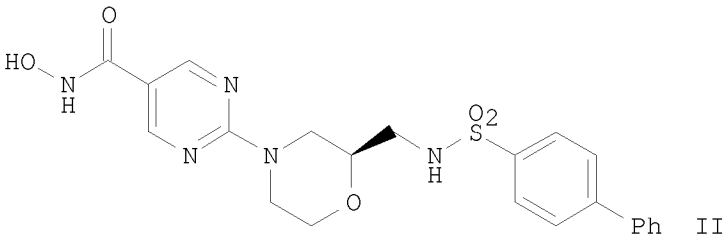


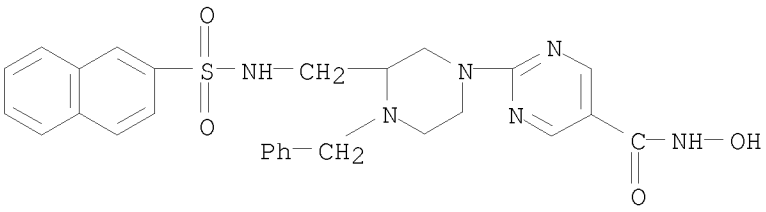
II

AB The title compds. [I; t = 0-4; Q, X, Y = N, C; Z = NH, O, CH2; R1 = CONR3R4, NHCOR7, CO(alkanediyl)SR7, etc. (wherein R3, R4 = H, OH, alkyl, etc.; R7 = H, alkyl, alkylcarbonyl, etc.); R2 = H, OH, NH2, etc.; L = NR9CO, NR9SO2, NR9CH2 (R9 = H, alkyl, cycloalkyl, etc.); A = (un)substituted Ph, cycloalkyl, pyridyl, etc.], having histone deacetylase inhibiting enzymic activity, were prepared and formulated. E.g., a multi-step synthesis of (+)-II which showed pIC50 of 7.723 against HDAC, was given.

IT 604784-81-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-(piperazinylmethyl-, piperidinylmethyl- and morpholinylmethyl) sulfonamides and amides as novel inhibitors of histone deacetylase)

RN 604784-81-8 CAPLUS

CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[3-[[(2-naphthalenylsulfonyl)amino]methyl]-4-(phenylmethyl)-1-piperazinyl]- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:737723 CAPLUS
DOCUMENT NUMBER: 139:261309
TITLE: Preparation of N-hydroxy-5-piperazino(piperidino or diazepino)-2-pyrimidinecarboxamides and N-hydroxy-4-piperazino(piperidino or diazepino)benzamides as new inhibitors of histone deacetylase
INVENTOR(S): Angibaud, Patrick Rene; Pilatte, Isabelle Noeelle Constance; Van Brandt, Sven Franciscus Anna; Roux, Bruno; Ten Holte, Peter; Verdonck, Marc Gustaaf Celine; Meerpoel, Lieven; Dyatkin, Alexey Borisovich
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

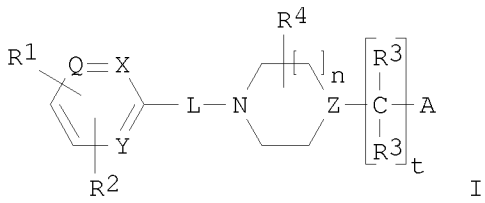
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076400	A1	20030918	WO 2003-EP2514	20030311
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2475764	A1	20030918	CA 2003-2475764	20030311
AU 2003218736	A1	20030922	AU 2003-218736	20030311
EP 1485353	A1	20041215	EP 2003-711980	20030311
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003008081	A	20041221	BR 2003-8081	20030311
CN 1639125	A	20050713	CN 2003-805675	20030311
CN 1642551	A	20050720	CN 2003-805833	20030311
NZ 534834	A	20050729	NZ 2003-534834	20030311
JP 2005526067	T	20050902	JP 2003-574621	20030311
CN 101007803	A	20070801	CN 2007-10005212	20030311
IN 2004DN02533	A	20070413	IN 2004-DN2533	20040831
US 20050107384	A1	20050519	US 2004-506998	20040908
ZA 2004007237	A	20050928	ZA 2004-7237	20040909
ZA 2004007235	A	20051004	ZA 2004-7235	20040909
ZA 2004007232	A	20051006	ZA 2004-7232	20040909
ZA 2004007233	A	20051006	ZA 2004-7233	20040909
ZA 2004007234	A	20051006	ZA 2004-7234	20040909
ZA 2004007236	A	20051006	ZA 2004-7236	20040909
MX 2004PA08806	A	20041126	MX 2004-PA8806	20040910
NO 2004004194	A	20041001	NO 2004-4194	20041001

PRIORITY APPLN. INFO.:		
US 2002-363799P	P	20020313
WO 2002-EP14833	A	20021223
CN 2003-805921	A3	20030311

WO 2003-EP2514 W 20030311

OTHER SOURCE(S): MARPAT 139:261309

GI



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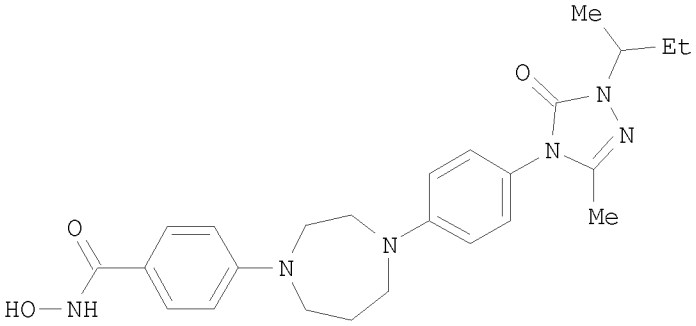


II

AB The title compds. [I; n = 0-3; t = 0-4; Q, X, Y = N, C; Z = N, CH; R1 = CONR7R8, NHCOR9, CO(alkanediyl)SR9, etc. (wherein R7, R8 = H, OH, alkyl, etc.; R9 = H, alkyl, alkylcarbonyl, etc.); R2 = H, halo, OH, etc.; L = a bond, alkanediyl, alkanediyloxy, NH, CO, NHCO; each R3 = H and one H atom can be replaced by aryl; R4 = H, OH, NH2, etc.; A = (un)substituted Ph, cyclohexyl, pyridyl, etc.], having histone deacetylase inhibiting enzymic activity, were prepared and formulated. E.g., a multi-step synthesis of II which showed pIC50 of 5.121 against HDAC, was given.

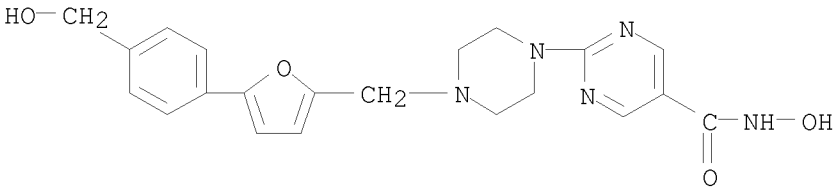
IT 603985-87-1P 603985-89-3P 603985-91-7P
603985-95-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazino(piperidino or diazepino) substituted 2-pyrimidinecarbohydroxamic acids and N-hydroxybenzamides as new inhibitors of histone deacetylase)

RN 603985-87-1 CAPLUS

CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[5-[4-(hydroxymethyl)phenyl]-2-furanyl]methyl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (5:4) (CA INDEX NAME)

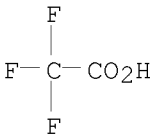
CM 1

CRN 603985-86-0
CMF C21 H23 N5 O4



CM 2

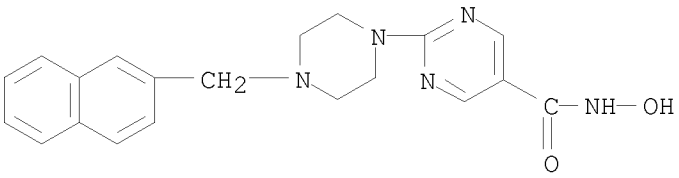
CRN 76-05-1
CMF C2 H F3 O2



RN 603985-89-3 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-naphthalenylmethyl)-1-piperazinyl]-, 2,2,2-trifluoroacetate (5:4) (CA INDEX NAME)

CM 1

CRN 603985-88-2
CMF C20 H21 N5 O2



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CRN 76-05-1
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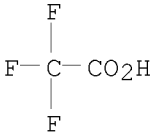
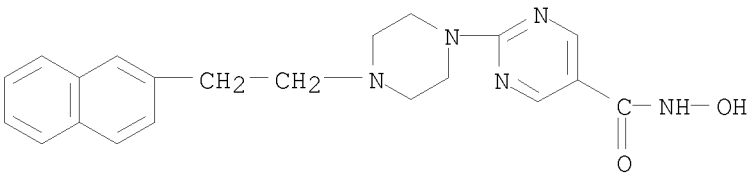


RN 603985-91-7 CAPLUS

CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[2-(2-naphthalenyl)ethyl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (5:4) (CA INDEX NAME)

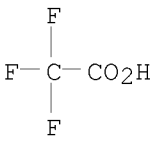
CM 1

CRN 603985-90-6
CMF C21 H23 N5 O2



CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 603985-95-1 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[5-[4-(4-morpholinylmethyl)phenyl]-2-furanyl]methyl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:2) (CA INDEX NAME)

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CRN 603985-94-0
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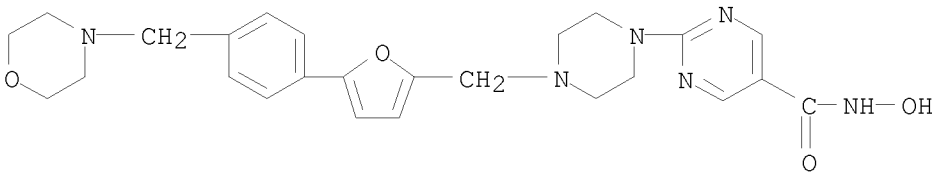
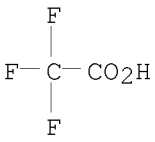
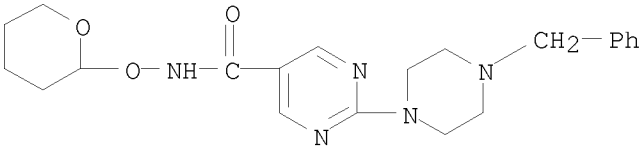


CM 2

CRN 76-05-1
CMF C2 H F3 O2



IT 603986-73-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperazino(piperidino or diazepino) substituted 2-pyrimidinecarbohydroxamic acids and N-hydroxybenzamides as new inhibitors of histone deacetylase)
RN 603986-73-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-(phenylmethyl)-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

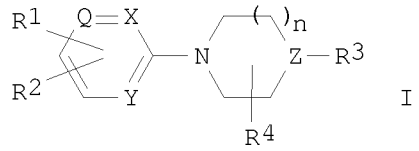
L3 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:737586 CAPLUS
DOCUMENT NUMBER: 139:261308
TITLE: Preparation of aryl and heteroaryl hydroxamic acids as inhibitors of histone deacetylase for treating proliferative diseases
INVENTOR(S): Van Emelen, Kristof; Verdonck, Marc Gustaaf Celine; Van Brandt, Sven Franciscus Anna; Angibaud, Patrick Rene; Meerpoel, Lieven; Dyatkin, Alexey Borisovich
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003075929	A1	20030918	WO 2003-EP2515	20030311
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2476065	A1	20030918	CA 2003-2476065	20030311
AU 2003218737	A1	20030922	AU 2003-218737	20030311
AU 2003218737	B2	20080410		
EP 1485099	A1	20041215	EP 2003-711981	20030311
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003007624	A	20050111	BR 2003-7624	20030311
CN 1639125	A	20050713	CN 2003-805675	20030311
CN 1642551	A	20050720	CN 2003-805833	20030311
JP 2005525379	T	20050825	JP 2003-574203	20030311
NZ 534832	A	20050930	NZ 2003-534832	20030311
CN 101007803	A	20070801	CN 2007-10005212	20030311
IN 2004DN02537	A	20070112	IN 2004-DN2537	20040831
ZA 2004007237	A	20050928	ZA 2004-7237	20040909
ZA 2004007235	A	20051004	ZA 2004-7235	20040909
ZA 2004007232	A	20051006	ZA 2004-7232	20040909
ZA 2004007233	A	20051006	ZA 2004-7233	20040909
ZA 2004007234	A	20051006	ZA 2004-7234	20040909
ZA 2004007236	A	20051006	ZA 2004-7236	20040909
MX 2004PA08797	A	20041126	MX 2004-PA8797	20040910
US 20050096468	A1	20050505	US 2004-507785	20040913
NO 2004004113	A	20040928	NO 2004-4113	20040928

PRIORITY APPLN. INFO.:	US 2002-363799P	P	20020313
	WO 2002-EP14833	A	20021223
	CN 2003-805921	A3	20030311
	WO 2003-EP2515	W	20030311

OTHER SOURCE(S): MARPAT 139:261308

GI



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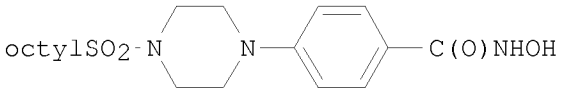


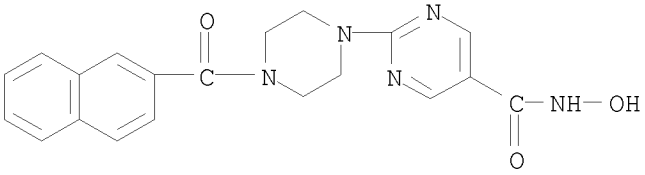
II

AB This invention comprises aryl and heteroaryl hydroxamic acids (shown as I; variables defined below; e.g. II) having histone deacetylase inhibiting enzymic activity; their preparation, compns. containing them and their use as a medicine. Compds. I show excellent in-vitro histone deacetylase inhibiting enzymic activity, have advantageous properties with regard to cellular activity and specific properties with regard to inhibition of cell cycle progression at both G1 and G2 checkpoints (p21 induction capacity), and show good metabolic stability and high bioavailability and more particular show oral bioavailability. They can also be used for detection and identification of histone deacetylase. General synthetic procedures and characterization data for twenty-seven I are included; also, prepns. of 12 intermediates are included. For example, a 59 % yield of 2-[4-(dimethylaminosulfonyl)piperazin-1-yl]pyrimidine-5-carbohydroxamic acid was obtained by removing the O-tetrahydropyranyl group of its ester using trifluoroacetic acid; the ester was prepared in 61 % yield from N'-(ethylcarbonimidoyl)-N,N-dimethyl-1,3-propanediamine monohydrochloride, sodium 2-[4-(dimethylaminosulfonyl)piperazin-1-yl]pyrimidine-5-carboxylate, O-(tetrahydro-2H-pyran-2-yl)hydroxylamine, and 1-hydroxy-1H-benzotriazole in CH2Cl2/THF. The sodium salt was obtained by base hydrolysis of the Et ester; the ester was prepared in 73 % yield from Et 2-(piperazin-1-yl)pyrimidine-5-carboxylate and dimethylsulfamoyl chloride; Et 2-(piperazin-1-yl)pyrimidine-5-carboxylate was obtained in <96 % yield from Et 2-(4-benzylpiperazin-1-yl)pyrimidine-5-carboxylate by hydrogenation using Pd/C; the benzyl derivative was obtained from 1-(phenylmethyl)piperazine, (135 mL) was added gradually to a solution of potassium carbonate (0.18 mol) and 2-(methylsulfonyl)-5-pyrimidinecarboxylic acid Et ester, K2CO3 in MeCN. For I: n is 0-3; Q, X and Y are N or C; Z is N or CH; R1 is -C(O)NR5R6, -N(H)C(O)R7, -C(O)-C1-6alkanediylSR7, -NR8C(O)N(OH)R7, -NR8C(O)C1-6alkanediylSR7, -NR8C(O)C:N(OH)R7 or another Zn-chelating-group; R2 is H, halo, hydroxy, amino, nitro, C1-6alkyl, C1-6alkyloxy, trifluoromethyl, di(C1-6-alkyl)amino, hydroxyamino or naphthalenylsulfonylpyrazinyl. R3 is H, C1-6-alkyl, arylC2-6alkenediyl, furanylcarbonyl, naphthalenylcarbonyl, -C(O)phenylR9, C1-6alkylaminocarbonyl, aminosulfonyl, arylaminosulfonyl, aminosulfonylamino, di(C1-6-alkyl)aminosulfonylamino, arylaminosulfonylamino, aminosulfonylaminoC1-6-alkyl, di(C1-6-alkyl)aminosulfonylaminoC1-6-alkyl, arylaminosulfonylaminoC1-6alkyl, di(C1-6-alkyl)aminoC1-6alkyl, Cl1-12-alkylsulfonyl, di(C1-6-alkyl)aminosulfonyl, trihaloC1-6-alkylsulfonyl, di(aryl)C1-6alkylcarbonyl, thiophenylC1-6alkylcarbonyl, pyridinylcarbonyl or arylC1-6alkylcarbonyl. R4 is H, hydroxy, amino, hydroxyC1-6alkyl, C1-6alkyl, C1-6alkyloxy,

arylC1-6alkyl, aminocarbonyl, hydroxycarbonyl, aminoC1-6-alkyl, aminocarbonylC1-6-alkyl, hydroxycarbonylC1-6-alkyl, hydroxyaminocarbonyl, C1-6-alkyloxycarbonyl, C1-6-alkylaminoC1-6-alkyl or di(C1-6-alkyl)aminoC1-6-alkyl; when R3 and R4 are present on the same C atom, R3 and R4 together may form -C(O)-NH-CH2-NR10- wherein R10 is H or aryl; when R3 and R4 are present on adjacent C atoms, R3 and R4 together may form :CH-CH:CH-CH: ; addnl. details are given in the claims.

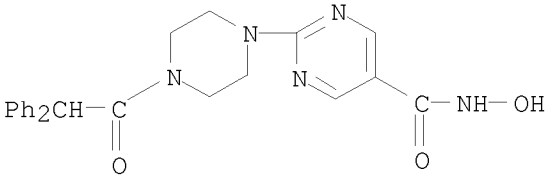
IT 603991-96-4P
RL: ARG (Analytical reagent use); PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate and reagent for detection/identification of histone deacetylase; preparation of aryl and heteroaryl hydroxamic acids as inhibitors of histone deacetylase for treating proliferative diseases)

RN 603991-96-4 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-naphthalenylcarbonyl)-1-piperazinyl]- (CA INDEX NAME)



IT 603991-95-3P 603992-24-1P 603992-25-2P
603992-26-3P 603992-27-4P 603992-28-5P
RL: ARG (Analytical reagent use); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate and reagent for detection/identification of histone deacetylase; preparation of aryl and heteroaryl hydroxamic acids as inhibitors of histone deacetylase for treating proliferative diseases)

RN 603991-95-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-(2,2-diphenylacetyl)-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



RN 603992-24-1 CAPLUS
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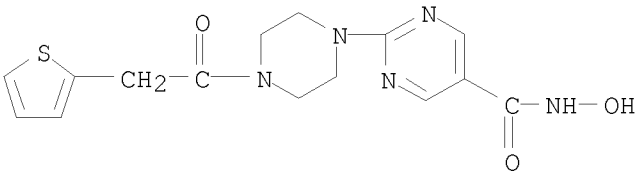

RN 603992-25-2 CAPLUS
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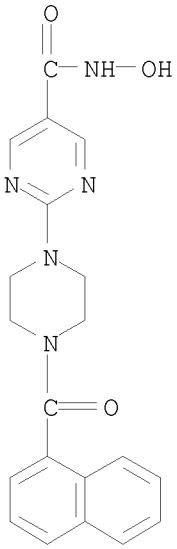
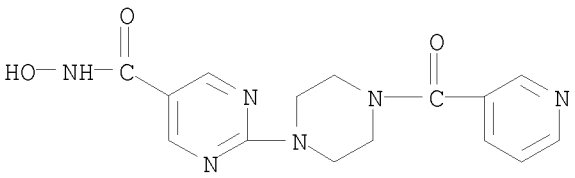
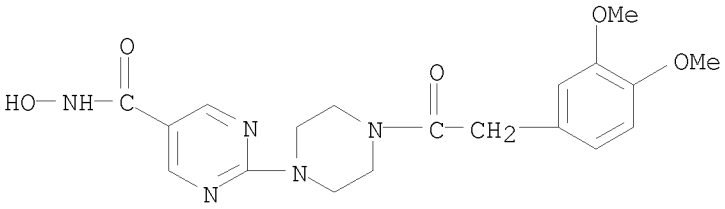


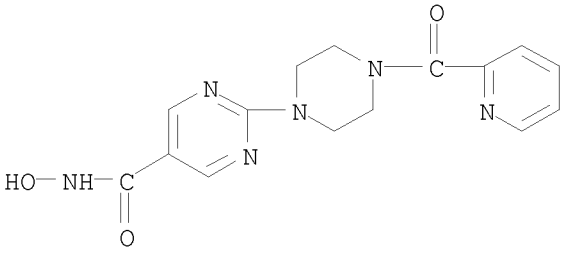
RN 603992-26-3 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(3-pyridinylcarbonyl)-1-piperazinyl]- (CA INDEX NAME)



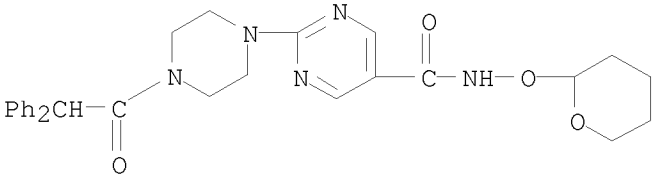
RN 603992-27-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[2-(3,4-dimethoxyphenyl)acetyl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



RN 603992-28-5 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-pyridinylcarbonyl)-1-piperazinyl]- (CA INDEX NAME)



IT 603992-32-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aryl and heteroaryl hydroxamic acids as inhibitors of histone deacetylase for treating proliferative diseases)
RN 603992-32-1 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-(2,2-diphenylacetyl)-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)

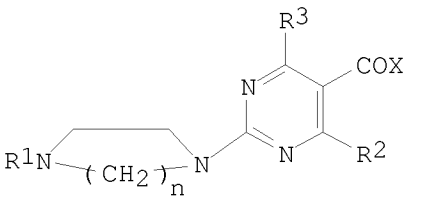


REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1986:442843 CAPLUS
DOCUMENT NUMBER: 105:42843
ORIGINAL REFERENCE NO.: 105:7101a,7104a
TITLE: Pyrimidinylpiperazines
INVENTOR(S): Kihara, Noriaki; Ishida, Tatsukazu; Isayama, Shigeru; Ishitoku, Takeshi; Tan, Hiroaki; Takahashi, Katsuya
PATENT ASSIGNEE(S): Mitsui Petrochemical Industries, Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 28 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 61043173	A	19860301	JP 1984-163771	19840806
JP 05022702	B	19930330		

PRIORITY APPLN. INFO.: JP 1984-163771 19840806
GI



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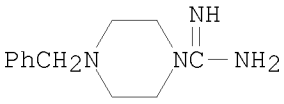
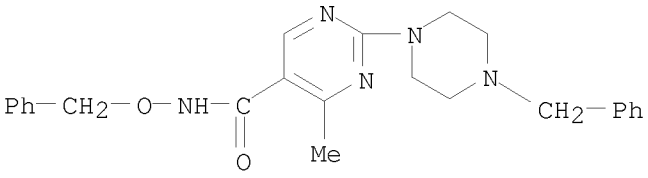


II

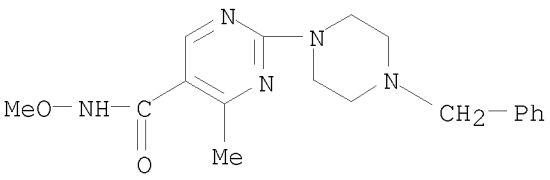
AB The title compds. [I, R1 = H, substituted Me, alkoxycarbonyl; R2, R3 = H, substituted alkyl; X = alkoxy, OH, (substituted) NH2; n = 2, 3], useful as herbicides against common weeds (no data), were prepared Thus, the piperazinecarboxamidine derivative II sulfate reacted with MeOCH:C(COMe)CO2Me in MeOH/aqueous NaOH at room temperature overnight to give 88% I (R1 = PhCH2, n = 2, R2 = H, R3 = Me, X = OMe).

IT 102976-25-0P 102976-32-9P
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as herbicide)

RN 102976-25-0 CAPLUS
CN 5-Pyrimidinecarboxamide, 4-methyl-N-(phenylmethoxy)-2-[4-(phenylmethyl)-1-piperazinyl]- (CA INDEX NAME)



RN 102976-32-9 CAPLUS
CN 5-Pyrimidinecarboxamide, N-methoxy-4-methyl-2-[4-(phenylmethyl)-1-piperazinyl]- (CA INDEX NAME)



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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                      60.43     239.00

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                      -8.80      -8.80

FILE 'REGISTRY' ENTERED AT 16:02:33 ON 15 SEP 2008
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STRUCTURE FILE UPDATES:   14 SEP 2008  HIGHEST RN 1049627-95-3
DICTIONARY FILE UPDATES:  14 SEP 2008  HIGHEST RN 1049627-95-3

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TSCA INFORMATION NOW CURRENT THROUGH July 5, 2008.

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10506998jason.str
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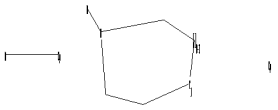
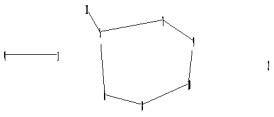




chain nodes :
1 2 4 11
ring nodes :
5 6 7 8 9 10
chain bonds :
1-4 5-11
ring bonds :
5-6 5-7 6-8 7-9 8-10 9-10
exact/norm bonds :
1-4 5-6 5-7 5-11 6-8 7-9 8-10 9-10

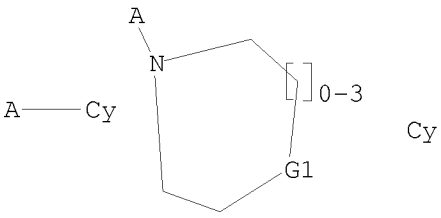
G1:C,N

Match level :
1:Atom 2:Atom 4:CLASS 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:CLASS
Generic attributes :
1:
Saturation   : Unsaturated
Number of Carbon Atoms : less than 7
Type of Ring System   : Monocyclic

Element Count :
Node 1: Limited
    C,C3-6
    N,N0-3

L4 STRUCTURE UPLOADED

=> d l4
L4 HAS NO ANSWERS
L4 STR



G1 C,N

Structure attributes must be viewed using STN Express query preparation.

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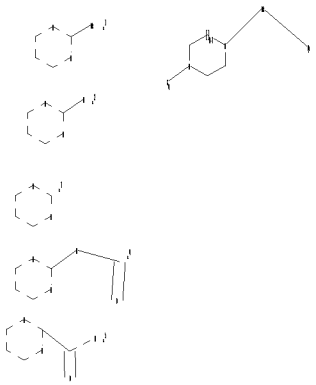
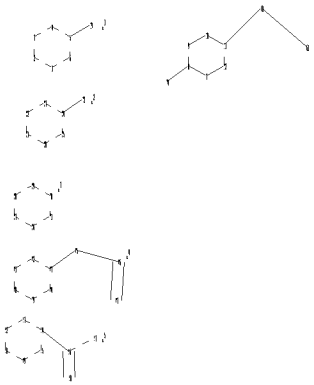
Uploading C:\Program Files\Stnexp\Queries\10506998election.str





chain nodes :
19 32 34 45 46 47 56 57 58 60 61
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 20 21 22 23 24 25 26 27 28 29 30
31 39 40 41 42 43 44 49 50 52 53 54 55
chain bonds :

<12/04/2007> Erich Leese

```
5-19  8-34  11-60  24-32  43-45  45-46  46-47  54-56  56-57  56-58  60-61
ring bonds :
1-2  1-6  2-3  3-4  4-5  5-6  7-8  7-12  8-9  9-10  10-11  11-12  20-21  20-25
21-22  22-23  23-24  24-25  26-27  26-31  27-28  28-29  29-30  30-31  39-40  39-44
40-41  41-42  42-43  43-44  49-50  49-55  50-52  52-53  53-54  54-55
exact/norm bonds :
1-2  1-6  2-3  3-4  4-5  5-6  5-19  7-8  7-12  8-9  8-34  9-10  10-11  11-12  11-60
 20-21  20-25  21-22  22-23  23-24  24-25  24-32  26-27  26-31  27-28  28-29  29-30
 30-31  39-40  39-44  40-41  41-42  42-43  43-44  43-45  45-46  46-47  49-50  49-55
 50-52  52-53  53-54  54-55  56-57  56-58  60-61
exact bonds :
54-56
isolated ring systems :
containing 1 : 7 : 20 : 26 : 39 : 49 :


G1:C,N

G2:Ak,NH2,NO2

G3:O

G4:[*1],[*2],[*3],[*4],[*5]

Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:Atom  19:CLASS  20:Atom  21:Atom  22:Atom  23:Atom  24:Atom  25:Atom
26:Atom  27:Atom  28:Atom  29:Atom  30:Atom  31:Atom  32:CLASS  34:CLASS  39:Atom
40:Atom  41:Atom  42:Atom  43:Atom  44:Atom  45:CLASS  46:CLASS  47:CLASS  49:Atom
50:Atom  52:Atom  53:Atom  54:Atom  55:Atom  56:CLASS  57:CLASS  58:CLASS  60:CLASS
 61:Atom



L5      STRUCTURE UPLOADED

=> d l5
L5 HAS NO ANSWERS
L5              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.


=> s l5 full
FULL SEARCH INITIATED 16:04:21 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -   596714 TO ITERATE

100.0% PROCESSED   596714 ITERATIONS                          10223 ANSWERS
SEARCH TIME: 00.00.08

L6        10223 SEA SSS FUL L5

=> file caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
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	ENTRY	SESSION
FULL ESTIMATED COST	179.28	418.28

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-8.80

FILE 'CAPLUS' ENTERED AT 16:04:37 ON 15 SEP 2008
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FILE COVERS 1907 - 15 Sep 2008 VOL 149 ISS 12
FILE LAST UPDATED: 14 Sep 2008 (20080914/ED)

Caplus now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2008.

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/legal/infopolicy.html

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=> s l6 full
L7        4042 L6

=> s l7 and py<2003
      22958911 PY<2003
L8        2880 L7 AND PY<2003
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=> file reg
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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	3.56	421.84

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-8.80

FILE 'REGISTRY' ENTERED AT 16:06:14 ON 15 SEP 2008
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STRUCTURE FILE UPDATES: 14 SEP 2008 HIGHEST RN 1049627-95-3
DICTIONARY FILE UPDATES: 14 SEP 2008 HIGHEST RN 1049627-95-3

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TSCA INFORMATION NOW CURRENT THROUGH July 5, 2008.

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

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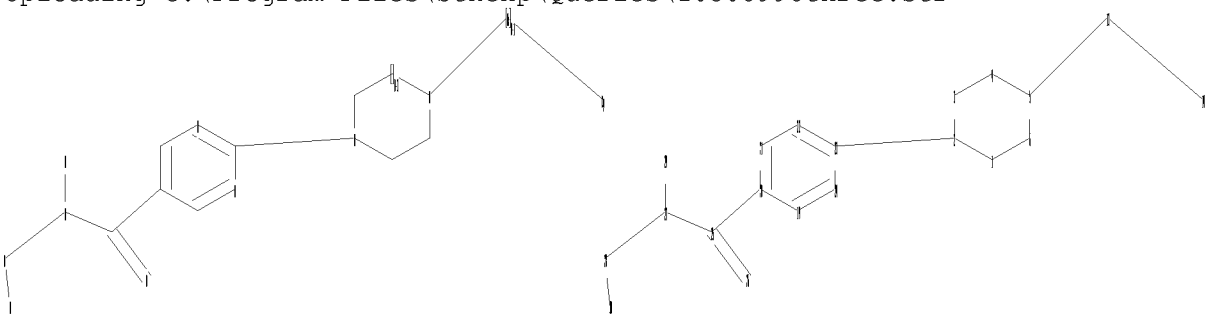

chain nodes :
13 14 25 26 27 28 29 30
ring nodes :
1 2 3 4 5 6 19 20 21 22 23 24
chain bonds :
2-23 5-13 13-14 20-25 25-26 25-27 27-28 27-29 28-30
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 19-20 19-24 20-21 21-22 22-23 23-24
exact/norm bonds :
1-2 1-6 2-3 2-23 3-4 4-5 5-6 5-13 13-14 25-26 25-27 27-28
exact bonds :
20-25 27-29 28-30
normalized bonds :
19-20 19-24 20-21 21-22 22-23 23-24
isolated ring systems :
containing 1 :

G1:C,N

G2:Ak,NH2,NO2

G3:O

<12/04/2007> Erich Leese

G4

G5:C,N,Zn,H

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 13:CLASS 14:Atom 19:Atom 20:Atom 21:Atom 22:Atom 23:Atom 24:Atom 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 30:CLASS

L9 STRUCTURE UPLOADED

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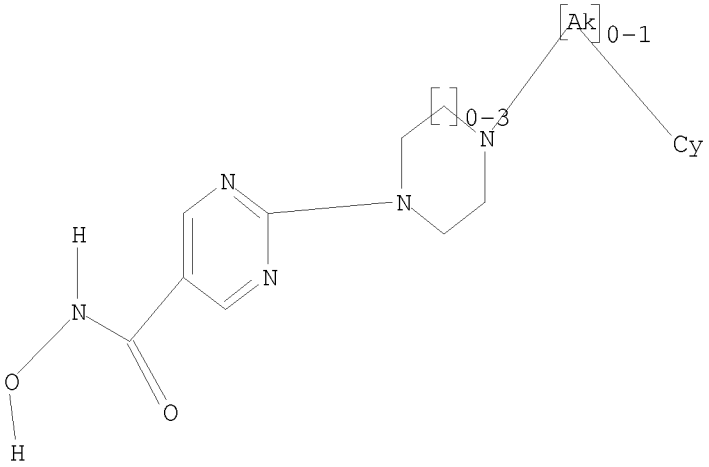
L9 HAS NO ANSWERS
L9 STR



G1 C,N

G2 Ak,NH2,NO2

G3 O

G4

G5 C,N,Zn,H

Structure attributes must be viewed using STN Express query preparation.

=> s l9 full
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FULL SCREEN SEARCH COMPLETED - 433 TO ITERATE

100.0% PROCESSED 433 ITERATIONS 112 ANSWERS
SEARCH TIME: 00.00.01

L10 112 SEA SSS FUL L9

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	178.82	600.66

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-8.80

FILE 'CAPLUS' ENTERED AT 16:07:34 ON 15 SEP 2008
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FILE COVERS 1907 - 15 Sep 2008 VOL 149 ISS 12
FILE LAST UPDATED: 14 Sep 2008 (20080914/ED)

Caplus now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2008.

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/legal/infopolicy.html

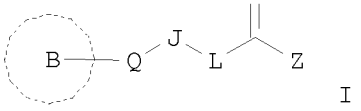
```
=> s l10 full
L11         13 L10

=> d ibib abs hitstr tot
```

L11 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:556979 CAPLUS
DOCUMENT NUMBER: 148:538314
TITLE: Preparation of tricyclic hydroxamic acids as inhibitors of histone deacetylase
INVENTOR(S): Shapiro, Gideon; Moncuso, John; Pierre, Tessier; Leit, Silvana; Deziel, Robert; David, Smil; Richard, Chesworth; Chantigny, Yves Andre; Patrick, Beaulieu
PATENT ASSIGNEE(S): Methygene Inc., Can.; En Vivo Pharmaceuticals, Inc.
SOURCE: PCT Int. Appl., 405pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2008055068	A2	20080508	WO 2007-US82668		20071026
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 20080207590	A1	20080828	US 2007-925151		20071026
PRIORITY APPLN. INFO.:			US 2006-863347P	P	20061028
			US 2007-884287P	P	20070110

OTHER SOURCE(S): MARPAT 148:538314
GI



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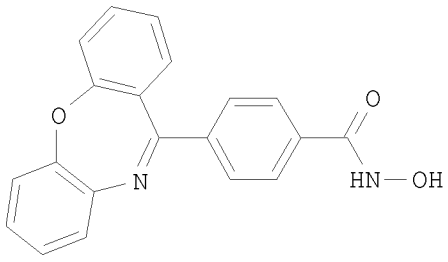


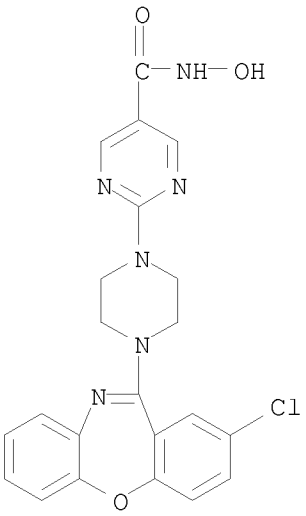
II

AB The title compds. I [Z = N(R1)OR2, H; L = a bond, N(OR2); when L = N(OR2), Z = H; when Z = H, L = N(OR2); R1, R2 = H, alkyl, aryl, etc.; J = a bond, :CH-, alkyl, alkyl(heteroalkyl)alkyl, etc.; Q = diazepine, pyrrolidine, diazabicyclo[3.3.1]nonane, etc.; B = dibenzo[b,f][1,4]oxazepine, benzo[b]pyrido[2,3-e][1,4]diazepine, benzo[f]thieno[2,3-b][1,4]oxazepine, etc.;], useful for the inhibition of histone deacetylase, were prepared E.g., a 3-step synthesis of II, starting from 10,11-

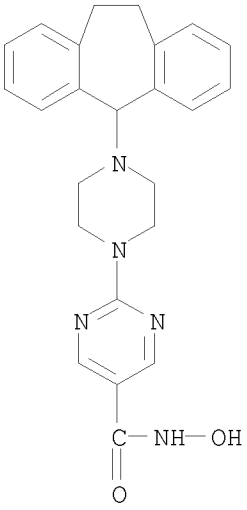
dihydrodibenz[b,f][1,4]oxazepin-11-one, was given. All exemplified compds. I have an IC50 of ≤ 10 μM against one of more of HDAC-1 through HDAC-11 (data for representative compds. I were given). Pharmaceutical composition comprising the compound I and methods of treating polyglutamine (polyQ) expansion diseases such as Huntington's disease, are disclosed.

IT 1024007-45-1P 1024009-50-4P 1024009-80-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tricyclic hydroxamic acids as inhibitors of histone deacetylase)

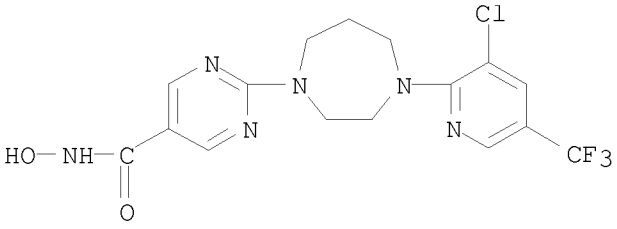
RN 1024007-45-1 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-(2-chlorodibenz[b,f][1,4]oxazepin-11-yl)-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



RN 1024009-50-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-yl)-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



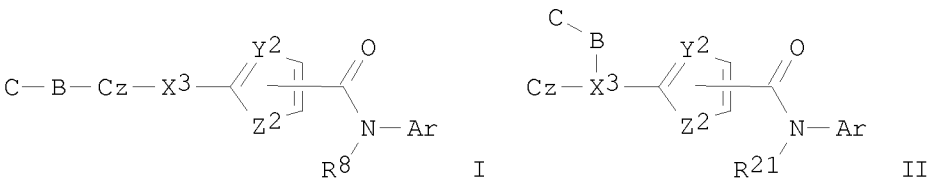
RN 1024009-80-0 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3-chloro-5-(trifluoromethyl)-2-pyridinyl]hexahydro-1H-1,4-diazepin-1-yl]-N-hydroxy- (CA INDEX NAME)



L11 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:353109 CAPLUS
DOCUMENT NUMBER: 148:379651
TITLE: Pyrimidine derivatives as tyrosine kinase inhibitors containing a zinc binding moiety and their preparation
INVENTOR(S): Cai, Xiong; Qian, Changgeng; Gould, Stephen; Zhai, Haixiao
PATENT ASSIGNEE(S): Curis, Inc., USA
SOURCE: PCT Int. Appl., 81pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

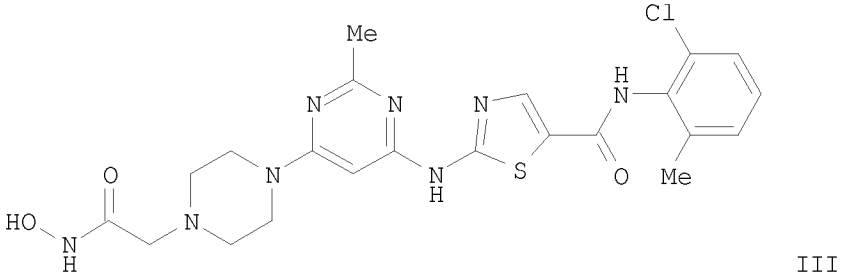
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008033746	A2	20080320	WO 2007-US77970	20070910
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 20080125440	A1	20080529	US 2007-852450	20070910
PRIORITY APPLN. INFO.:			US 2006-843730P P	20060911
			US 2007-895901P P	20070320

OTHER SOURCE(S): MARPAT 148:379651
GI



I

II



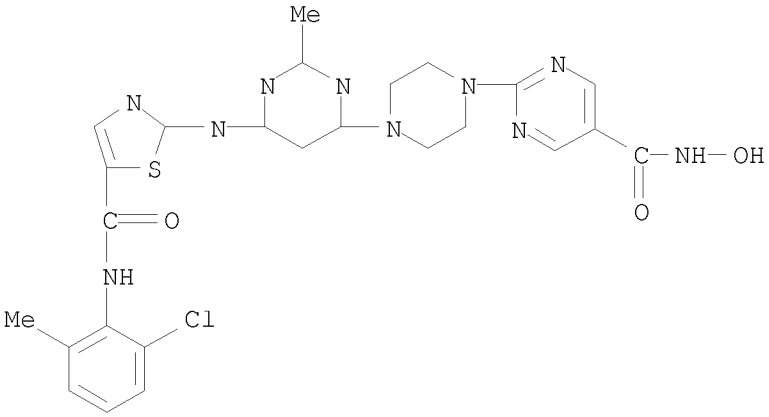
III

AB The invention relates to tyrosine kinase inhibitors of formula I and II that contain a zinc-binding moiety and their use in the treatment of tyrosine related diseases and disorders such as cancer. The said derivs. may further act as HDAC inhibitors. Compds. of formula I and II wherein Cz is (un)substituted (hetero)aryl, and (un)substituted heterocyclic; Ar is (un)substituted (hetero)aryl; X3 is NH, alkylamino, O, and S; Z2 is O, S, NH and alkylamino; Y2 is N, CH, C-halo, C-(hetero)aryl, etc.; R21 is H and aliphatic; B is a liner. C is urea, thiourea, acetyl, thioacetyl, etc.; R8 is H, acyl, and (un)substituted aliphatic group; and their geometric isomers, enantiomers, diastereoisomers, racemates, pharmaceutically acceptable salts, and solvates thereof, are claimed. Example compound III was prepared by a multistep procedure (procedure given). All the invention compds. were evaluated for their tyrosine kinase inhibitory activity.

IT 1012886-07-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyrimidine derivs. as tyrosine kinase inhibitors containing a zinc binding moiety)

RN 1012886-07-5 CAPLUS

CN 5-Pyrimidinecarboxamide, 2-[4-[6-[[5-[[(2-chloro-6-methylphenyl)amino]carbonyl]-2-thiazolyl]amino]-2-methyl-4-pyrimidinyl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)

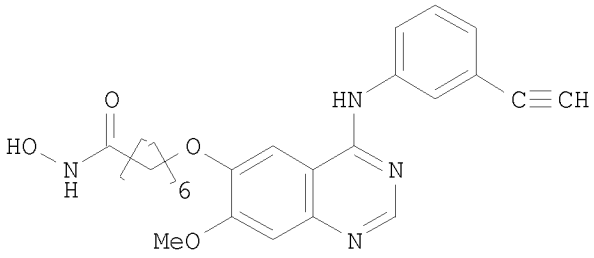


ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L11 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:353001 CAPLUS
DOCUMENT NUMBER: 148:355828
TITLE: Multi-functional small molecules as anti-proliferative agents and their preparation
INVENTOR(S): Cai, Xiong; Qian, Changgeng; Gould, Stephen; Zhai, Haixiao
PATENT ASSIGNEE(S): Curis, Inc., USA
SOURCE: PCT Int. Appl., 494pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008033747	A2	20080320	WO 2007-US77971	20070910
WO 2008033747	A9	20080724		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA			
US 20080221132	A1	20080911	US 2007-852458	20070910

PRIORITY APPLN. INFO.: US 2006-843590P P 20060911
US 2007-895889P P 20070320
OTHER SOURCE(S): MARPAT 148:355828
GI



A—B—C I II

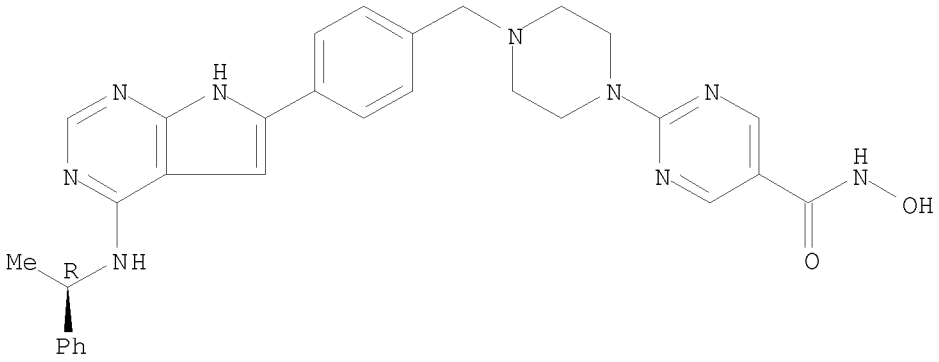
AB The invention relates to the compns., methods, and applications of an approach to selective inhibition of several cellular or mol. targets with a single small mol. More specifically, the present invention relates to multi-functional small mols. of formula I wherein one functionality is capable of inhibiting histone deacetylases (HDAC) and the other

functionality is capable of inhibiting a different cellular or mol. pathway involved in aberrant cell proliferation, differentiation or survival. Compds. of formula I wherein A is a pharmacophore of an anticancer agent capable of inhibiting at least one cellular or mol. pathway involved in the aberrant cell proliferation, differentiation or survival; B is a linker; C is a zinc-binding moiety; and their geometrical isomers, enantiomers, diastereoisomers, racemates, pharmaceutically acceptable salts, prodrugs and solvates thereof, are claimed. Example compound II was prepared by a multistep procedure (procedure given). All the invention compds. were evaluated for their antiproliferative activity (some data given).

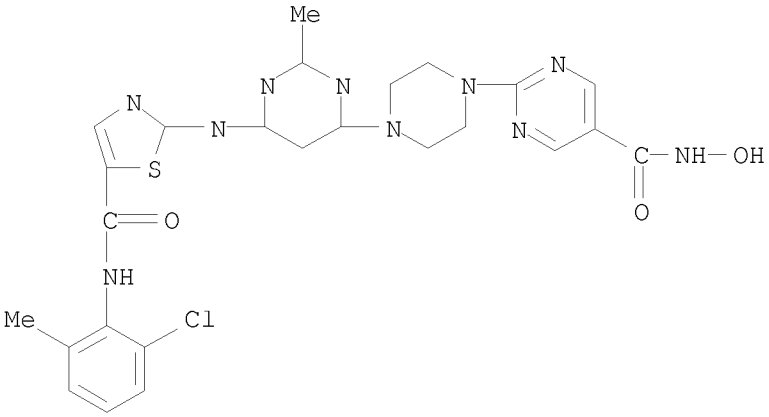
IT 1011716-90-7P 1012886-07-5P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRPH (Prophetic); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prophetic starting material; preparation of multi-functional small mols. as antiproliferative agents)

RN 1011716-90-7 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[4-[4-[[(1R)-1-phenylethyl]amino]-7H-pyrrolo[2,3-d]pyrimidin-6-yl]phenyl]methyl]-1-piperazinyl]- (CA INDEX NAME)

Absolute stereochemistry.



RN 1012886-07-5 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[6-[[5-[[(2-chloro-6-methylphenyl)amino]carbonyl]-2-thiazolyl]amino]-2-methyl-4-pyrimidinyl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L11 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:351928 CAPLUS
DOCUMENT NUMBER: 148:355814
TITLE: Preparation of (aralkylamino)(phenyl)pyrrolo[2,3-d]pyrimidine derivatives for use as protein tyrosine kinase (PTK) inhibitors
INVENTOR(S): Cai, Xiong; Qian, Changgeng; Gould, Stephen
PATENT ASSIGNEE(S): Curis, Inc., USA
SOURCE: PCT Int. Appl., 123pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008033745	A2	20080320	WO 2007-US77968	20070910
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 20080161320	A1	20080703	US 2007-852440	20070910
PRIORITY APPLN. INFO.:			US 2006-843646P P	20060911
			US 2007-895894P P	20070320

OTHER SOURCE(S): MARPAT 148:355814
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

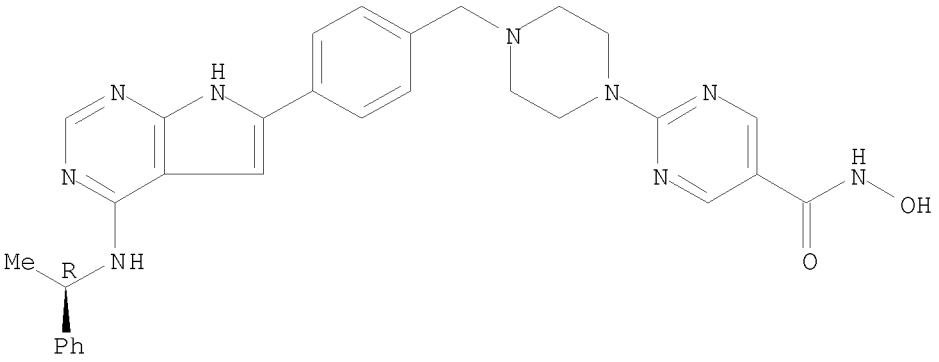
AB Fused bicyclic pyrimidine derivs. I and II [Ar = aryl, substituted arylheteroaryl or heteroaryl; Q = absent or (un)substituted alkyl; X = O, S, NH, or alkylamino; Z = O, S, NR1; Y = N or CR2; B = linker; D = C(O)NH2, NHC(S)CH3, CHC(O)NHacyl, etc.; R1 = H or (un)substituted alkyl; R2 = H, halo, (un)substituted aliphatic, aryl or heteroaryl], and their pharmaceutically acceptable salts, are prepared and disclosed as protein tyrosine kinase (PTK) inhibitors. Thus, e.g., III was prepared by N-alkylation of 1,4-dioxa-8-azaspiro[4.5]decane with 6-(4-(chloromethyl)phenyl)-N-((R)-1-phenylethyl)-7H-pyrrolo[2,3-d]pyrimidin-4-amine (preparation given) and deprotection followed by condensation with 6-aminohexanoic acid Me ester and amidation with hydroxylamine. Select I were evaluated in EGFR assays, e.g., III demonstrated an IC50 value of ≤0.1 (μM).
IT 1011716-90-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(preparation of (aralkylamino)(phenyl)pyrrolopyrimidine derivs. for use as protein tyrosine kinase (PTK) inhibitors)

RN 1011716-90-7 CAPLUS

CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[4-[4-[[(1R)-1-phenylethyl]amino]-7H-pyrrolo[2,3-d]pyrimidin-6-yl]phenyl]methyl]-1-piperazinyl]- (CA INDEX NAME)

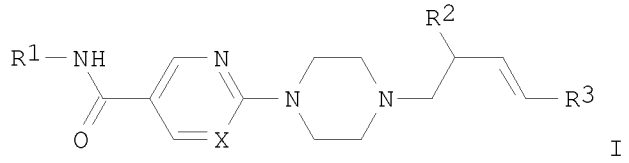
Absolute stereochemistry.



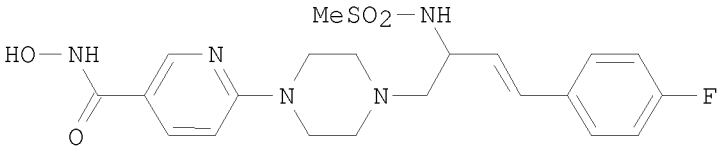
L11 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:816930 CAPLUS
DOCUMENT NUMBER: 147:211903
TITLE: Preparation of pyrimidine derivatives as histone deacetylase inhibitors
INVENTOR(S): Marconnet-Decrane, Laurence Francoise Bernadette; Gaurrand, Sandrine Francoise Dominique; Angibaud, Patrick Rene
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 62pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2007082874	A1	20070726	WO 2007-EP50371		20070116
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW					
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
CA 2630717	A1	20070726	CA 2007-2630717		20070116
PRIORITY APPLN. INFO.:			EP 2006-100570	A	20060119
			WO 2007-EP50371	W	20070116

OTHER SOURCE(S): MARPAT 147:211903
GI



I



F_3CCO_2H II

<12/04/2007> Erich Leese

AB The title compds. with general formula I [wherein R1 = OH or substituted phenyl; X = N or CH; R2 = amino, alkylamino, alkoxyl, OH, etc.; R3 = (un)substituted Ph, naphthalene, or heterocycle] or N-oxide forms, pharmaceutically acceptable salts, or stereoisomeric forms thereof were prepared as histone deacetylase (HDAC) inhibitors for the treatment of proliferative diseases. For example, compound II was prepared in a multi-step synthesis. In vitro assay for inhibition of HDAC was performed to measure the inhibition of HDAC enzymic activity, and colorimetric assay was performed to determine cellular activity on A2780 tumor cells. II showed HDAC inhibitory and anti-proliferative activities in the above two assays with pIC50 values of 7.0 and 5.3, resp. Formulations containing I as active ingredients were also reported.

IT 944738-91-4P 944738-94-7P 944738-97-0P
944739-00-8P 944739-08-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyrimidine derivs. as histone deacetylase inhibitors)

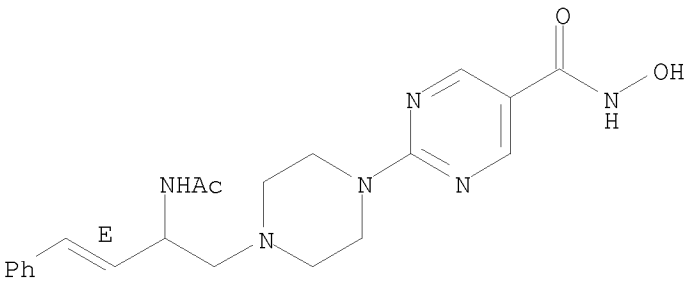
RN 944738-91-4 CAPLUS

CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-(acetylamino)-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

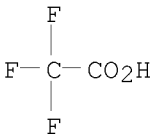
CRN 944738-90-3
CMF C21 H26 N6 O3

Double bond geometry as shown.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

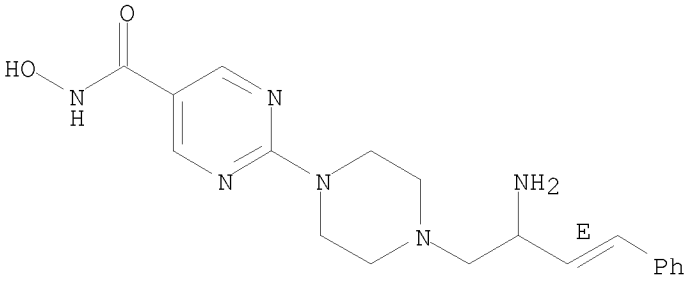


RN 944738-94-7 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-amino-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

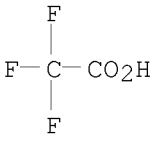
CRN 944738-93-6
CMF C19 H24 N6 O2

Double bond geometry as shown.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

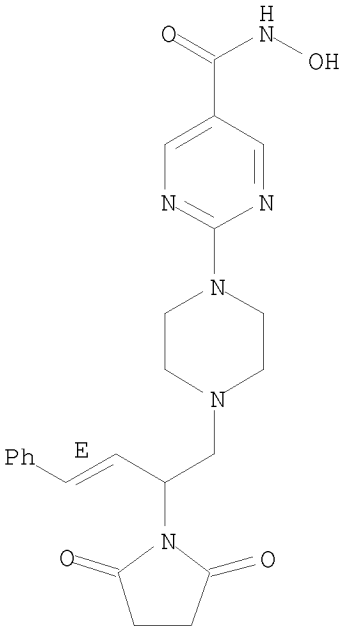


RN 944738-97-0 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-(2,5-dioxo-1-pyrrolidinyl)-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

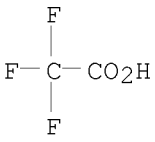
CRN 944738-96-9
CMF C23 H26 N6 O4

Double bond geometry as shown.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

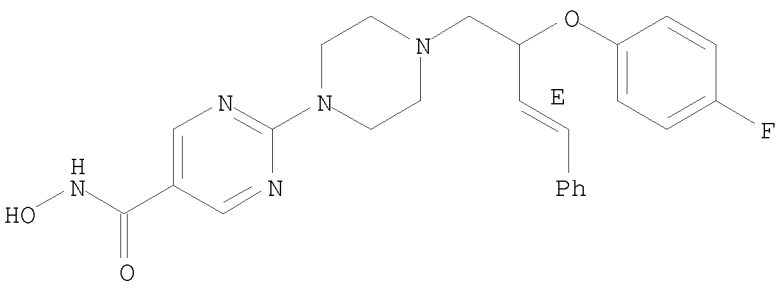


RN 944739-00-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-(4-fluorophenoxy)-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

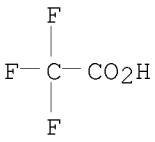
CRN 944738-99-2
CMF C25 H26 F N5 O3

Double bond geometry as shown.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

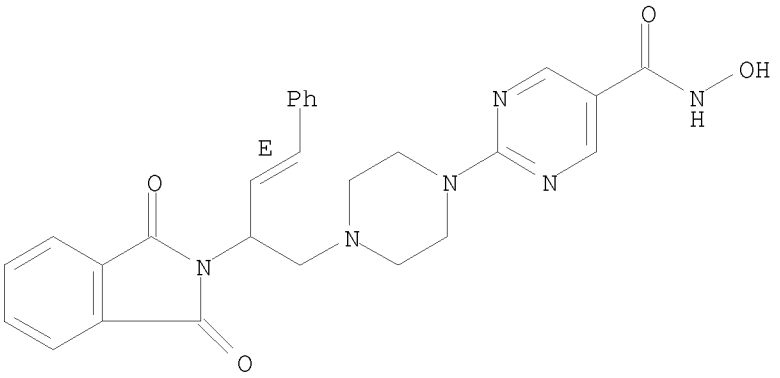


RN 944739-08-6 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

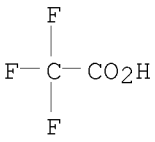
CRN 944739-07-5
CMF C27 H26 N6 O4

Double bond geometry as shown.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

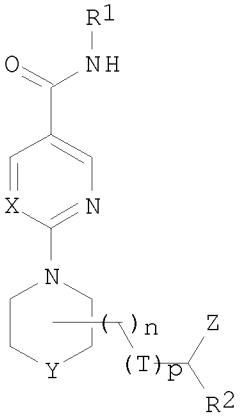


REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:816806 CAPLUS
DOCUMENT NUMBER: 147:211902
TITLE: Preparation of pyrimidine derivatives as histone deacetylase inhibitors
INVENTOR(S): Angibaud, Patrick Rene; Van Brandt, Sven Franciscus Anna; Marconnet-Decrane, Laurence Francoise Bernadette; Roux, Bruno
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 63pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007082880	A1	20070726	WO 2007-EP50379	20070116
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: EP 2006-100571 A 20060119
OTHER SOURCE(S): MARPAT 147:211902
GI



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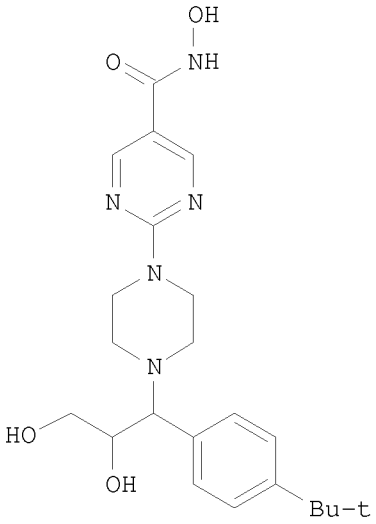


II

AB The title compds. with general formula I [wherein R1 = OH or substituted phenyl; R2 = -CH2OH, -CH2OCH3, -CH2OCH2CH3, or -CH2CH(OH)CH2OH; T = N(R3), where R3 = H, alkyl, cycloalkyl, etc.; X = N or CH; Y = O, NH, CH2, etc.; n = 0-1; p = 0-1, provided that when p = 0 then n = 0 and Y = N, and -CH(R2)-Z is attached to Y; Z = (un)substituted aryl or heteroaryl] or N-oxide forms, pharmaceutically acceptable salts, or stereoisomeric forms thereof were prepared as histone deacetylase (HDAC) inhibitors for the treatment of proliferative diseases. For example, compound II was prepared in a multi-step synthesis. In vitro assay for inhibition of HDAC was performed to measure the inhibition of HDAC enzymic activity, and colorimetric assay was performed to determine cellular activity on A2780 tumor cells. II showed HDAC inhibitory and anti-proliferative activities in the above two assays with pIC50 values of 7.0 and 7.1, resp. Formulations containing I as active ingredients were also reported.

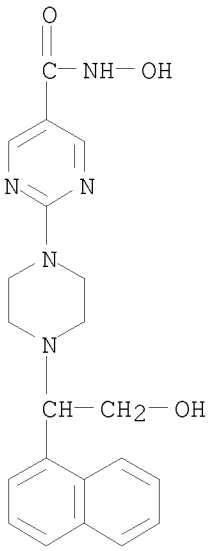
IT 944712-03-2P 944712-05-4P 944712-07-6P
944712-09-8P 944712-10-1P 944712-12-3P
944712-14-5P 944712-16-7P 944712-18-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyrimidine derivs. as histone deacetylase inhibitors)

RN 944712-03-2 CAPLUS

CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[2-hydroxy-1-(1-naphthalenyl)ethyl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

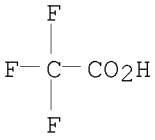
CM 1

CRN 944712-02-1
CMF C21 H23 N5 O3



CM 2

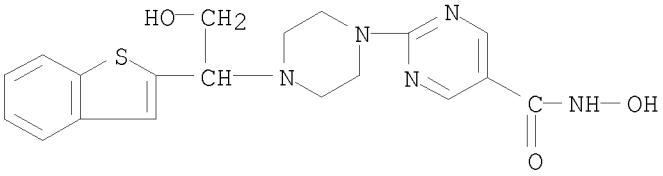
CRN 76-05-1
CMF C2 H F3 O2



RN 944712-05-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-(1-benzo[b]thien-2-yl-2-hydroxyethyl)-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

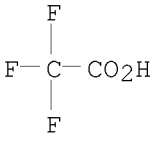
CM 1

CRN 944712-04-3
CMF C19 H21 N5 O3 S



CM 2

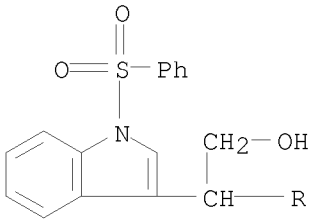
CRN 76-05-1
CMF C2 H F3 O2

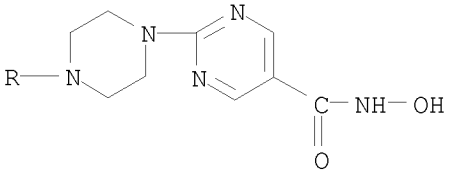


RN 944712-07-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[2-hydroxy-1-[1-(phenylsulfonyl)-1H-indol-3-yl]ethyl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

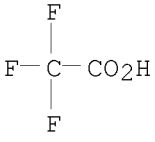
CRN 944712-06-5
CMF C25 H26 N6 O5 S





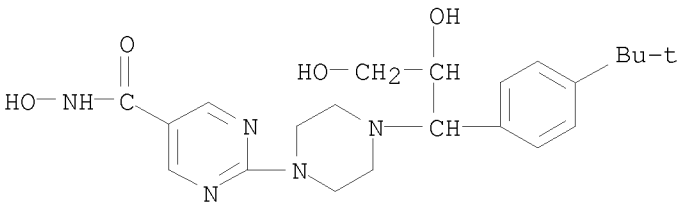
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 944712-09-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[4-(1,1-dimethylethyl)phenyl]-2,3-

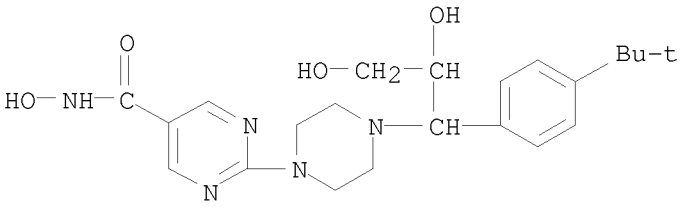
dihydroxypropyl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



RN 944712-10-1 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[4-(1,1-dimethylethyl)phenyl]-2,3-dihydroxypropyl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

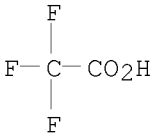
CM 1

CRN 944712-09-8
CMF C22 H31 N5 O4



CM 2

CRN 76-05-1
CMF C2 H F3 O2

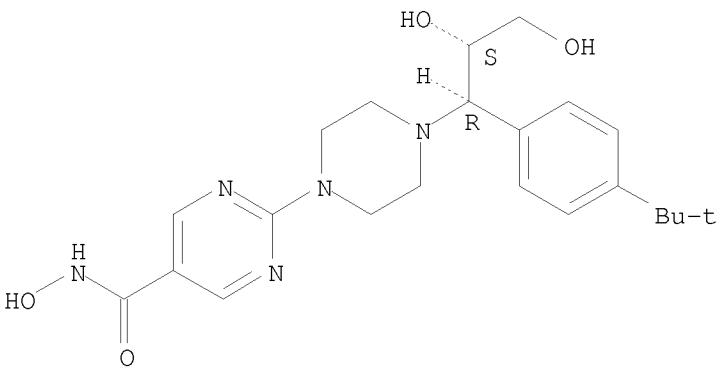


RN 944712-12-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(1R,2S)-1-[4-(1,1-dimethylethyl)phenyl]-2,3-dihydroxypropyl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

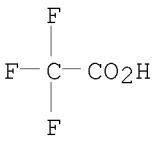
CRN 944712-11-2
CMF C22 H31 N5 O4

Absolute stereochemistry.



CM 2

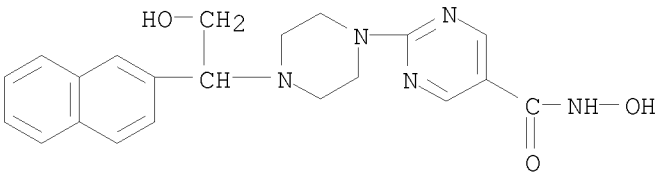
CRN 76-05-1
CMF C2 H F3 O2



RN 944712-14-5 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[2-hydroxy-1-(2-naphthalenyl)ethyl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

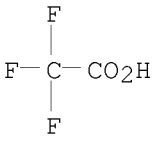
CM 1

CRN 944712-13-4
CMF C21 H23 N5 O3



CM 2

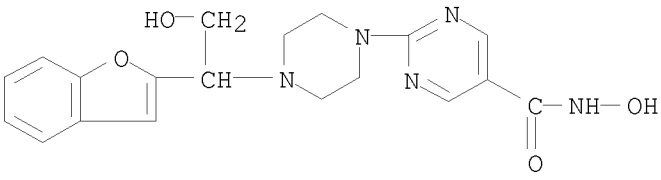
CRN 76-05-1
CMF C2 H F3 O2



RN 944712-16-7 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-(2-benzofuranyl)-2-hydroxyethyl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

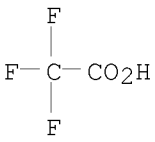
CM 1

CRN 944712-15-6
CMF C19 H21 N5 O4



CM 2

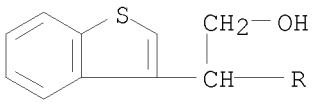
CRN 76-05-1
CMF C2 H F3 O2

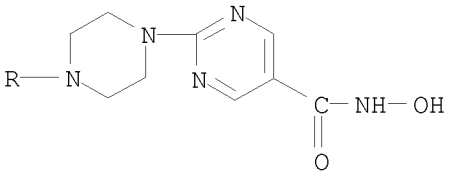


RN 944712-18-9 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-(1-benzo[b]thien-3-yl-2-hydroxyethyl)-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

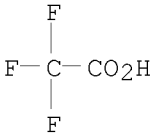
CRN 944712-17-8
CMF C19 H21 N5 O3 S





CM 2

CRN 76-05-1
CMF C2 H F3 O2



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:485854 CAPLUS
DOCUMENT NUMBER: 146:482095
TITLE: Preparation of squaric acid derivatives as histone deacetylase (HDAC) inhibitors for the treatment of proliferative diseases
INVENTOR(S): Van Emelen, Kristof
PATENT ASSIGNEE(S): Janssen Pharmaceutica N. V., Belg.
SOURCE: PCT Int. Appl., 37pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007048767	A1	20070503	WO 2006-EP67656	20061023
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2006307918	A1	20070503	AU 2006-307918	20061023
CA 2623360	A1	20070503	CA 2006-2623360	20061023
EP 1943232	A1	20080716	EP 2006-807466	20061023
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS				

PRIORITY APPLN. INFO.: EP 2005-110080 A 20051027
WO 2006-EP67656 W 20061023
OTHER SOURCE(S): MARPAT 146:482095
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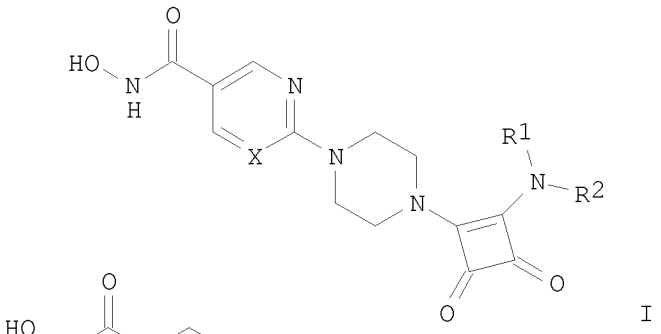

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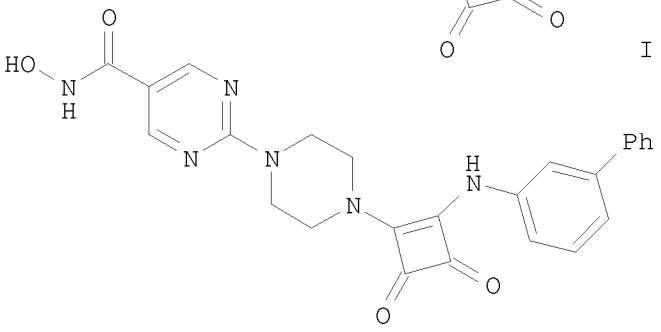


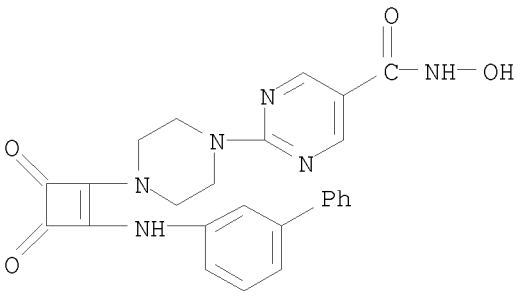
II

AB Title compds. I [wherein X = N or CH; R1, R2 = H, alkyl, Ph, etc.;] or N-oxides, pharmaceutically acceptable salts and stereoisomers thereof were prepared as histone deacetylase (HDAC) inhibitors. For instance, successive condensation of 3,4-diethoxy-3-cyclobutene-1,2-dione with 3-aminobiphenyl and 2-(1-piperazinyl)pyrimidine-5-carboxylic acid Et ester, ester hydrolysis, condensation of the resultant acid with NH2O-THP, and deprotection with TFA gave hydroxamic acid II. This compds. showed inhibition against HDAC with pIC50 = 7.7. The invented compds. are useful for the treatment of proliferative diseases.

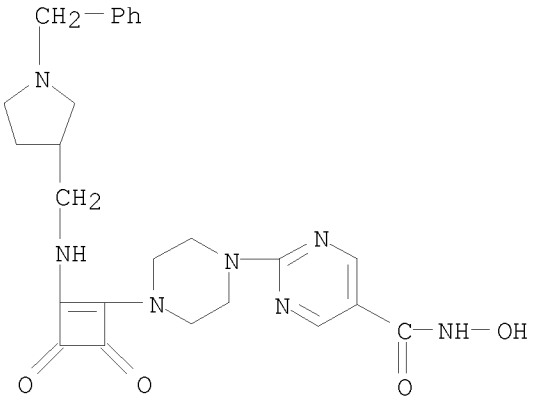
IT 935670-93-2P 935670-95-4P 935670-97-6P
935670-99-8P 935671-01-5P 935671-03-7P
935671-05-9P 935671-07-1P 935671-09-3P
935671-11-7P 935671-13-9P 935671-15-1P
935671-17-3P 935671-19-5P 935671-21-9P
935671-23-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of squaric acid derivs. as histone deacetylase (HDAC) inhibitors for treatment of proliferative diseases)

RN 935670-93-2 CAPLUS

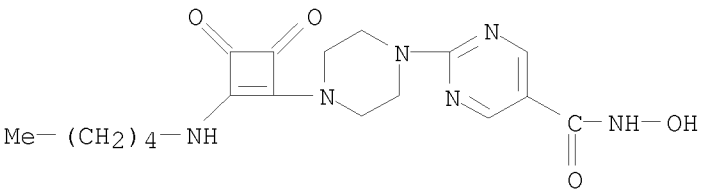
CN 5-Pyrimidinecarboxamide, 2-[4-[2-([1,1'-biphenyl]-3-ylamino)-3,4-dioxo-1-cyclobuten-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



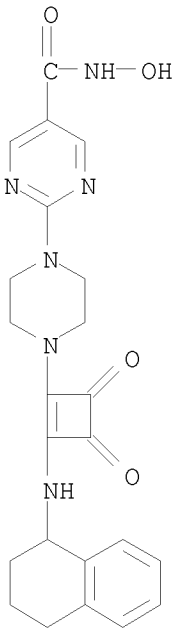
RN 935670-95-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3,4-dioxo-2-[[[1-(phenylmethyl)-3-pyrrolidinyl]methyl]amino]-1-cyclobuten-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



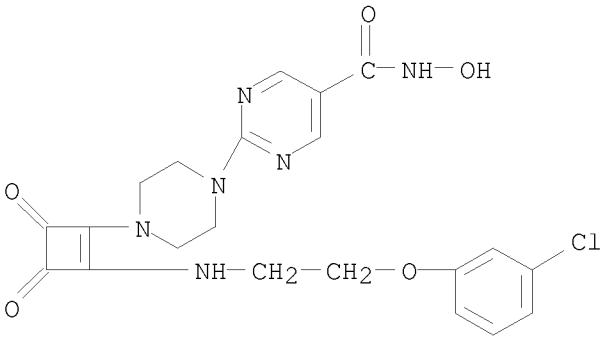
RN 935670-97-6 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3,4-dioxo-2-(pentylamino)-1-cyclobuten-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



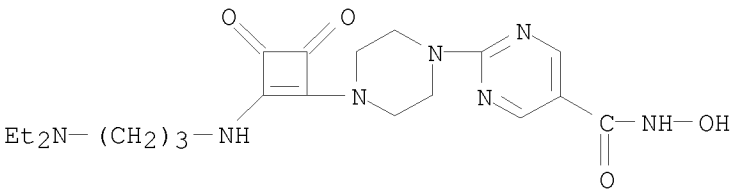
RN 935670-99-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3,4-dioxo-2-[(1,2,3,4-tetrahydro-1-naphthalenyl)amino]-1-cyclobuten-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



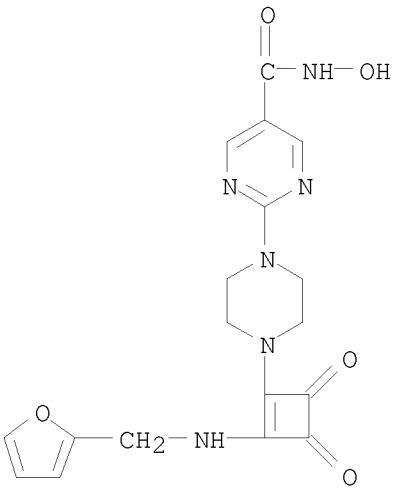
RN 935671-01-5 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[2-[[2-(3-chlorophenoxy)ethyl]amino]-3,4-dioxo-1-cyclobuten-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



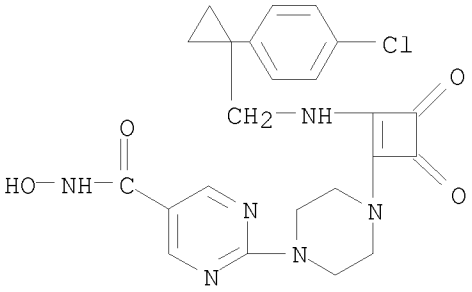
RN 935671-03-7 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[2-[[3-(diethylamino)propyl]amino]-3,4-dioxo-1-cyclobuten-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



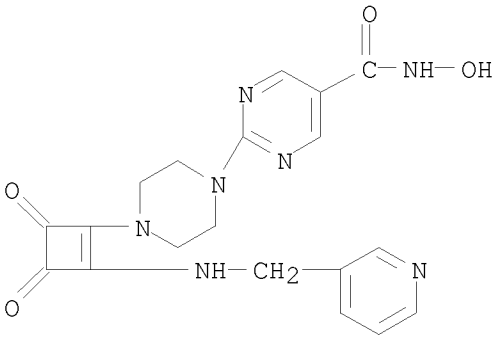
RN 935671-05-9 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[2-[(2-furanylmethyl)amino]-3,4-dioxo-1-cyclobuten-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



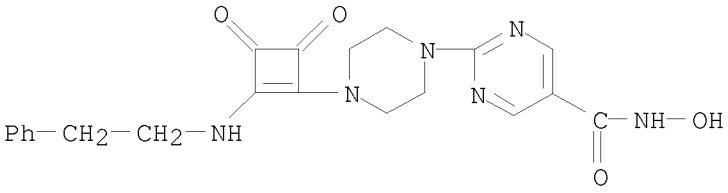
RN 935671-07-1 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[2-[[[1-(4-chlorophenyl)cyclopropyl]methyl]amino]-3,4-dioxo-1-cyclobuten-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



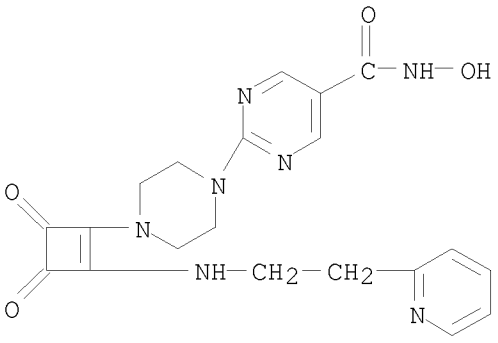
RN 935671-09-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3,4-dioxo-2-[(3-pyridinylmethyl)amino]-1-cyclobuten-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



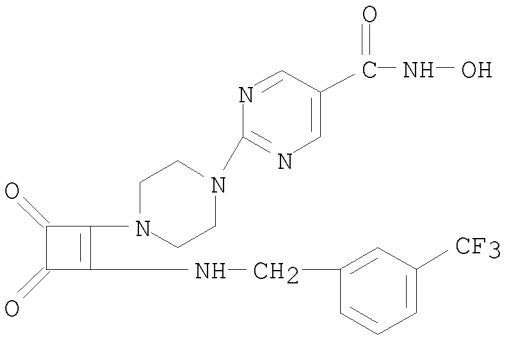
RN 935671-11-7 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3,4-dioxo-2-[(2-phenylethyl)amino]-1-cyclobuten-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



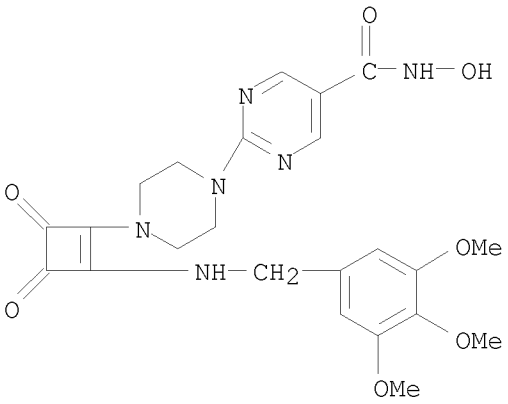
RN 935671-13-9 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3,4-dioxo-2-[[2-(2-pyridinyl)ethyl]amino]-1-cyclobuten-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



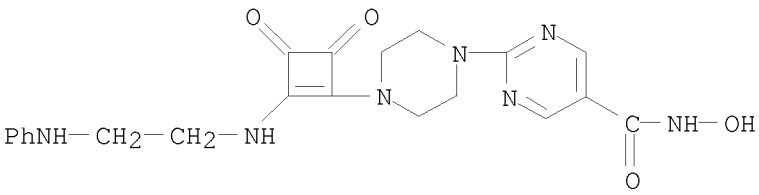
RN 935671-15-1 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3,4-dioxo-2-[[[3-(trifluoromethyl)phenyl]methyl]amino]-1-cyclobuten-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



RN 935671-17-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3,4-dioxo-2-[[(3,4,5-trimethoxyphenyl)methyl]amino]-1-cyclobuten-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)

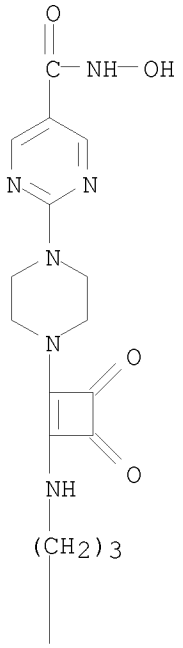


RN 935671-19-5 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3,4-dioxo-2-[[2-(phenylamino)ethyl]amino]-1-cyclobuten-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)

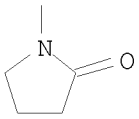


RN 935671-21-9 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3,4-dioxo-2-[[3-(2-oxo-1-pyrrolidinyl)propyl]amino]-1-cyclobuten-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)

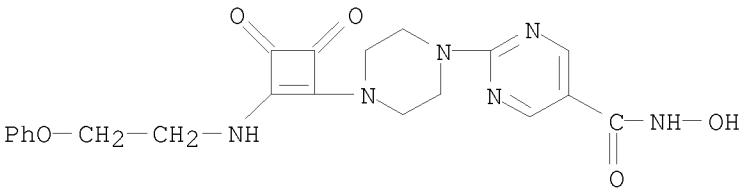
PAGE 1-A



PAGE 2-A



RN 935671-23-1 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3,4-dioxo-2-[(2-phenoxyethyl)amino]-1-cyclobuten-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:101446 CAPLUS
DOCUMENT NUMBER: 144:192266
TITLE: Preparation of substituted propenyl piperazine derivatives as novel inhibitors of histone deacetylase
INVENTOR(S): Van Brandt, Sven Franciscus Anna; Van Emelen, Kristof; Angibaud, Patrick Rene; Marconnet-Decrane, Laurence Francoise Bernadette; Arts, Janine
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2006010749	A2	20060202	WO 2005-EP53611		20050725
WO 2006010749	A3	20060608			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
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CA 2572971	A1	20060202	CA 2005-2572971		20050725
EP 1776358	A2	20070425	EP 2005-777776		20050725
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CN 1993356	A	20070704	CN 2005-80025487		20050725
JP 2008508234	T	20080321	JP 2007-523072		20050725
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KR 2007043978	A	20070426	KR 2007-701641		20070123
US 20070135424	A1	20070614	US 2007-626215		20070123
IN 2007DN00658	A	20070803	IN 2007-DN658		20070124
MX 200701119	A	20070315	MX 2007-1119		20070126
NO 2007001117	A	20070227	NO 2007-1117		20070227
PRIORITY APPLN. INFO.:			EP 2004-77171	A	20040728
			US 2004-592357P	P	20040729
			WO 2005-EP53611	W	20050725

OTHER SOURCE(S): CASREACT 144:192266; MARPAT 144:192266
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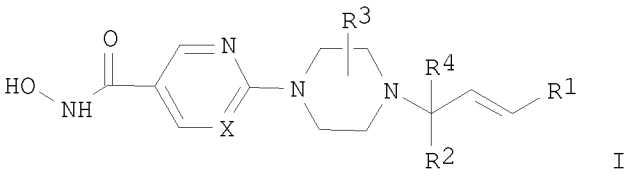

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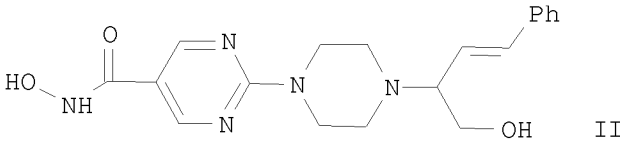

II

AB Substituted propenyl piperazine derivs. I, wherein X is independently N or CH; R1 is Ph, naphthalenyl or heterocyclyl; wherein each of said Ph or naphthalenyl is optionally substituted with one or two substituents each independently selected from halo, alkyl, alkyloxy, poly-halo-alkyl, aryl, hydroxy, cyano, amino, alkylcarbonylamino, alkylsulfonylamino, hydroxycarbonyl, alkyloxycarbonyl, hydroxyalkyl, alkyloxymethyl, aminomethyl, alkylaminomethyl, alkylcarbonylaminomethyl, alkylsulfonylaminomethyl, aminosulfonyl, alkylaminosulfonyl or heterocyclyl; R2 is hydrogen, -CH2R5, trifluoromethyl, -C(O)-R6, or -CH-NR7R8; wherein each R5 is independently hydrogen, hydroxy, alkyloxy, alkyloxyalkyloxy, alkylcarbonyloxy, piperazinyl, N-methylpiperazinyl, morpholinyl, thiomorpholinyl, imidazolyl or triazolyl; each R6 is independently hydroxy, alkyloxy, amino or mono- or di(alkyl)amino, cycloalkylamino, hydroxyalkylamino, piperazinyl, N-methylpiperazinyl, morpholinyl or thiomorpholinyl; each R7 and R8 are independently hydrogen, alkyl, alkylcarbonyl, alkylsulfonyl, or mono- or di(alkyl)aminosulfonyl; R3 is hydrogen, hydroxymethyl, aminomethyl or mono- or di(alkyl)aminomethyl; R4 is hydrogen or alkyl; were prepared and having histone deacetylase inhibiting enzymic activity and to inhibit proliferative conditions, such as cancer and psoriasis. Thus, propenyl piperazine derivative II was prepared and tested in vitro and in nude mice as inhibitor of histone deacetylase and was better than R306465 after oral administration. P21 enzyme linked immunosorbent assay has been applied to determine the p21 protein expression level in human A2780 ovarian carcinoma cells. In vitro assay for inhibition of histone deacetylase is reported. P21 induction was measured as the consequence of DNA damage or as the consequence of histone deacetylase inhibition. Antiproliferative activity of title compds. was determined on A2780 cells (neg. log value of the IC50, pIC50 = 7.9-8.2).

IT 875138-85-5P 875138-87-7P 875138-88-8P
875138-89-9P 875138-90-2P 875138-91-3P
875138-93-5P 875138-94-6P 875138-98-0P
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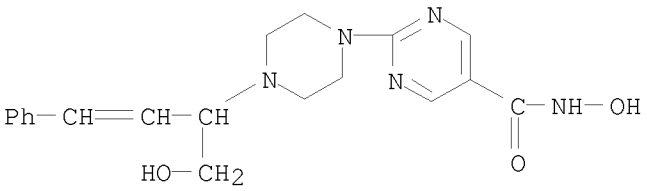
875139-30-3P 875139-31-4P 875139-69-8P

875139-70-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted propenyl piperazine derivs. as novel inhibitors of histone deacetylase)

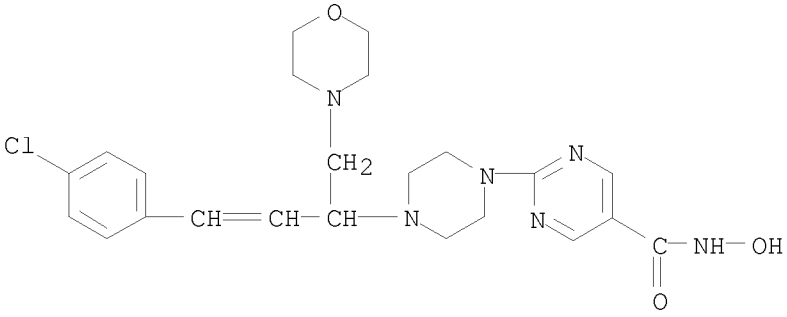
RN 875138-85-5 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(hydroxymethyl)-3-phenyl-2-propen-1-yl]-1-piperazinyl]- (CA INDEX NAME)



RN 875138-87-7 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3-(4-chlorophenyl)-1-(4-morpholinylmethyl)-2-propen-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

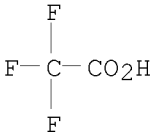
CM 1

CRN 875138-86-6
CMF C23 H29 Cl N6 O3



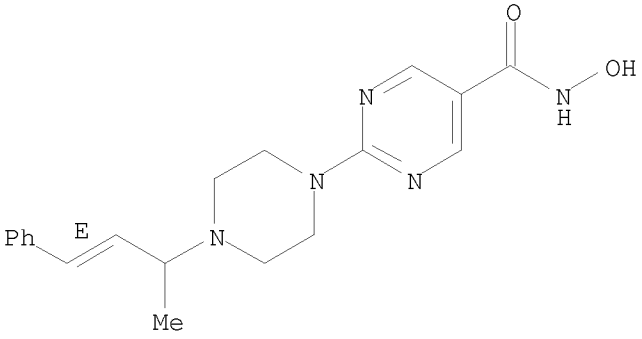
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 875138-88-8 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(2E)-1-methyl-3-phenyl-2-propen-1-yl]-1-piperazinyl]- (CA INDEX NAME)

Double bond geometry as shown.

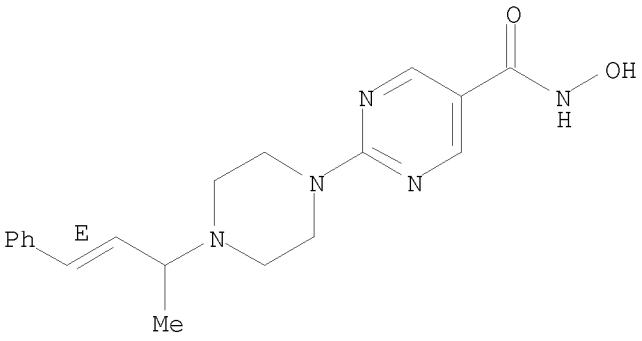


RN 875138-89-9 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(2E)-1-methyl-3-phenyl-2-propen-1-yl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

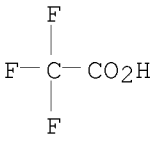
CRN 875138-88-8
CMF C19 H23 N5 O2

Double bond geometry as shown.

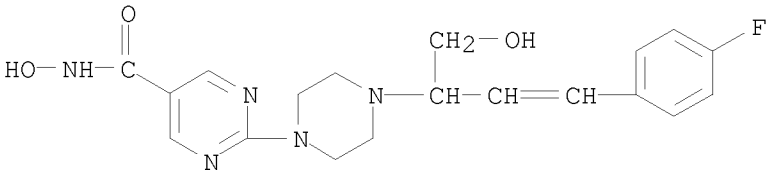


CM 2

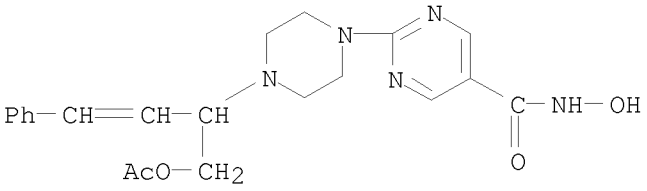
CRN 76-05-1
CMF C2 H F3 O2



RN 875138-90-2 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3-(4-fluorophenyl)-1-(hydroxymethyl)-2-propen-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



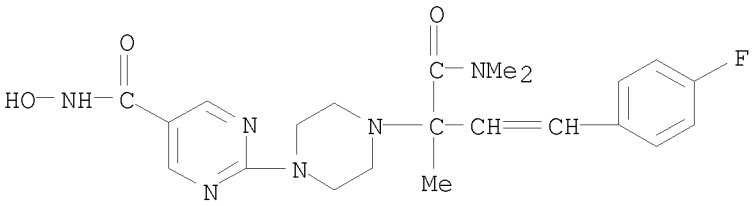
RN 875138-91-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[(acetyloxy)methyl]-3-phenyl-2-propen-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



RN 875138-93-5 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[(dimethylamino)carbonyl]-3-(4-fluorophenyl)-1-methyl-2-propen-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

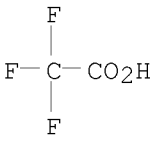
CM 1

CRN 875138-92-4
CMF C22 H27 F N6 O3

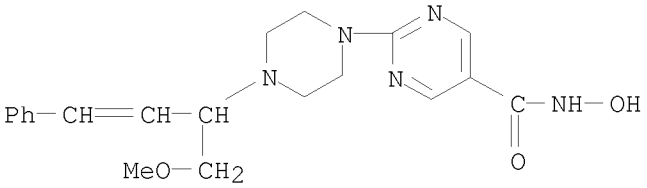


CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 875138-94-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(methoxymethyl)-3-phenyl-2-propen-1-yl]-1-piperazinyl]- (CA INDEX NAME)

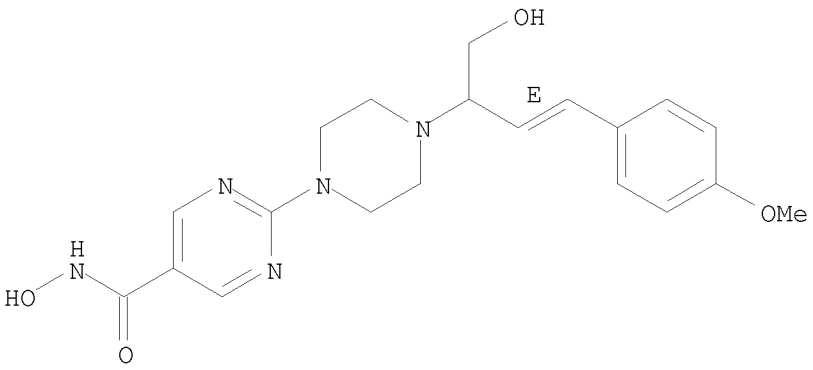


RN 875138-98-0 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(2E)-1-(hydroxymethyl)-3-(4-methoxyphenyl)-2-propen-1-yl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 875138-97-9
CMF C20 H25 N5 O4

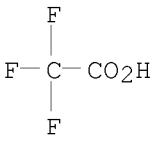
Double bond geometry as shown.



CM 2

CRN 76-05-1

CMF C2 H F3 O2

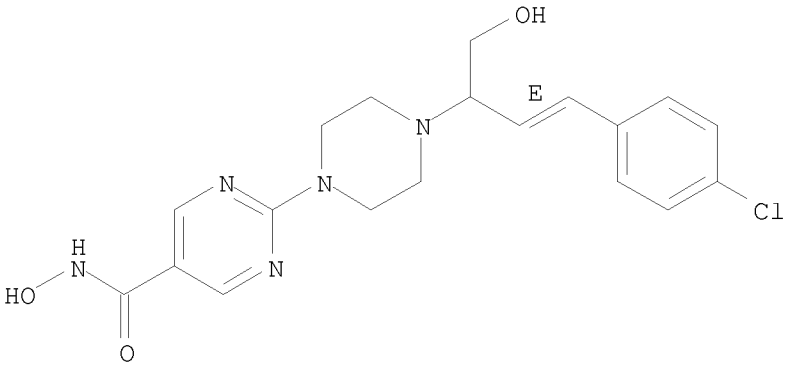


RN 875139-00-7 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(2E)-3-(4-chlorophenyl)-1-(hydroxymethyl)-2-propen-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 875138-99-1
CMF C19 H22 Cl N5 O3

Double bond geometry as shown.



CM 2

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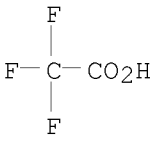
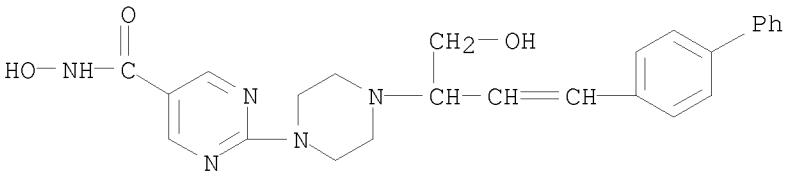


RN 875139-02-9 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3-[1,1'-biphenyl]-4-yl-1-(hydroxymethyl)-2-propen-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

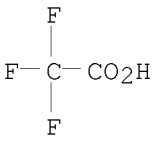
CM 1

CRN 875139-01-8
CMF C25 H27 N5 O3



CM 2

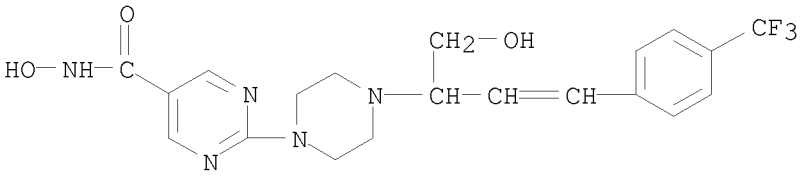
CRN 76-05-1
CMF C2 H F3 O2



RN 875139-04-1 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(hydroxymethyl)-3-[4-(trifluoromethyl)phenyl]-2-propen-1-yl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

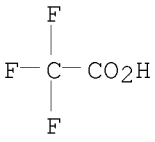
CM 1

CRN 875139-03-0
CMF C20 H22 F3 N5 O3



CM 2

CRN 76-05-1
CMF C2 H F3 O2

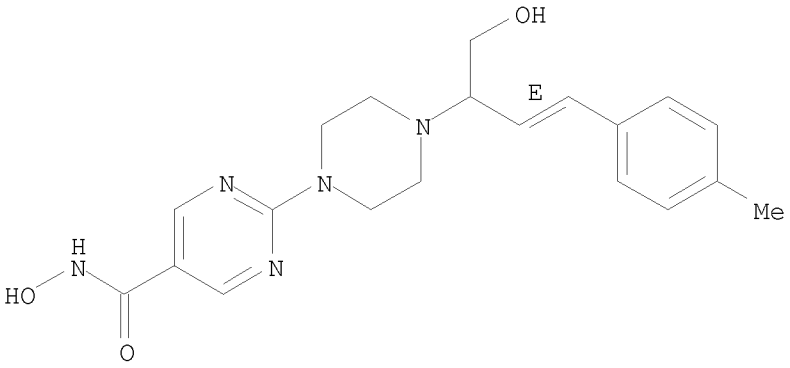


RN 875139-06-3 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(2E)-1-(hydroxymethyl)-3-(4-methylphenyl)-2-propen-1-yl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

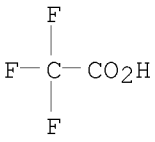
CRN 875139-05-2
CMF C20 H25 N5 O3

Double bond geometry as shown.

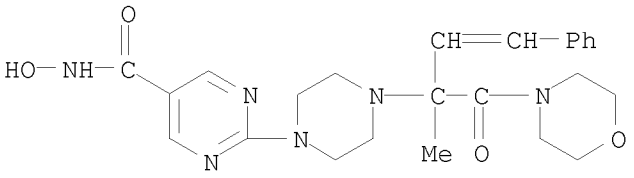


CM 2

CRN 76-05-1
CMF C2 H F3 O2



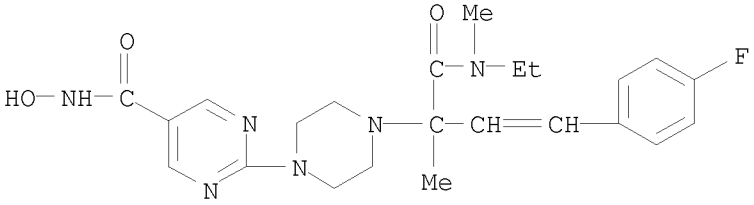
RN 875139-07-4 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-methyl-1-(4-morpholinylcarbonyl)-3-phenyl-2-propen-1-yl]-1-piperazinyl]- (CA INDEX NAME)



RN 875139-09-6 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[(ethylmethylamino)carbonyl]-3-(4-fluorophenyl)-1-methyl-2-propen-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

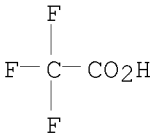
CM 1

CRN 875139-08-5
CMF C23 H29 F N6 O3



CM 2

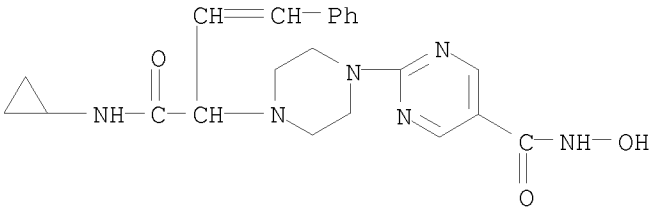
CRN 76-05-1
CMF C2 H F3 O2



RN 875139-11-0 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[(cyclopropylamino)carbonyl]-3-phenyl-2-propen-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

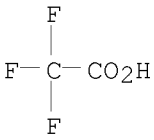
CM 1

CRN 875139-10-9
CMF C22 H26 N6 O3



CM 2

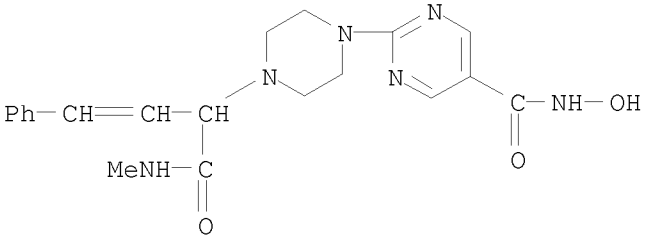
CRN 76-05-1
CMF C2 H F3 O2



RN 875139-13-2 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-[(methylamino)carbonyl]-3-phenyl-2-propen-1-yl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

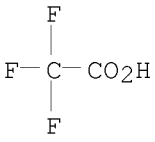
CM 1

CRN 875139-12-1
CMF C20 H24 N6 O3

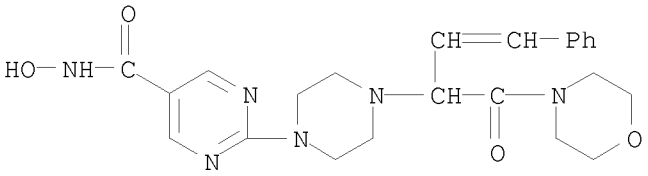


CM 2

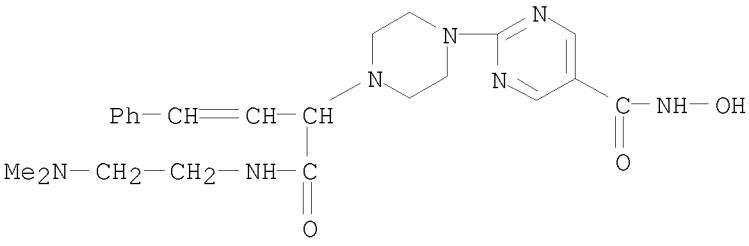
CRN 76-05-1
CMF C2 H F3 O2



RN 875139-14-3 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(4-morpholinylcarbonyl)-3-phenyl-2-propen-1-yl]-1-piperazinyl]- (CA INDEX NAME)



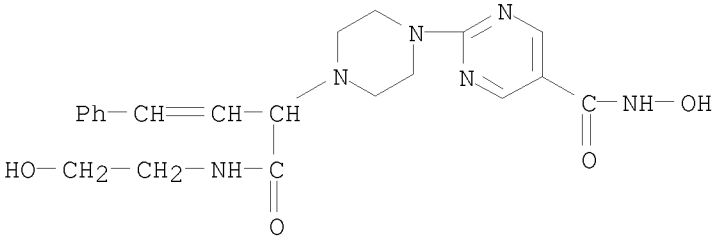
RN 875139-15-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[[[2-(dimethylamino)ethyl]amino]carbonyl]-3-phenyl-2-propen-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



RN 875139-17-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-[[(2-hydroxyethyl)amino]carbonyl]-3-phenyl-2-propen-1-yl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

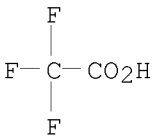
CM 1

CRN 875139-16-5
CMF C21 H26 N6 O4



CM 2

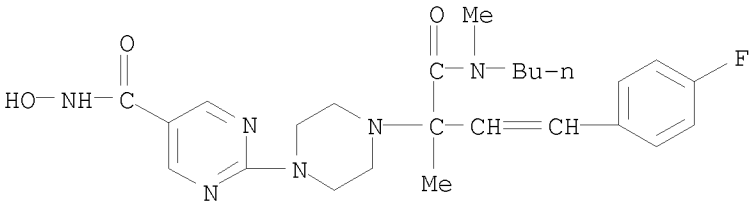
CRN 76-05-1
CMF C2 H F3 O2



RN 875139-19-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[(butylmethylamino)carbonyl]-3-(4-fluorophenyl)-1-methyl-2-propen-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

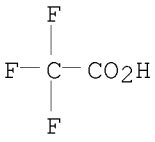
CM 1

CRN 875139-18-7
CMF C25 H33 F N6 O3

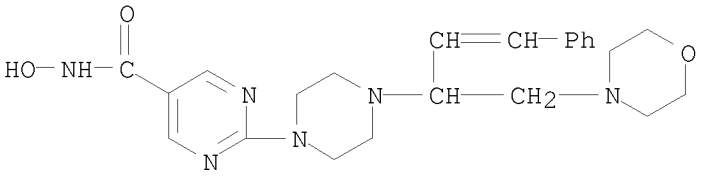


CM 2

CRN 76-05-1
CMF C2 H F3 O2

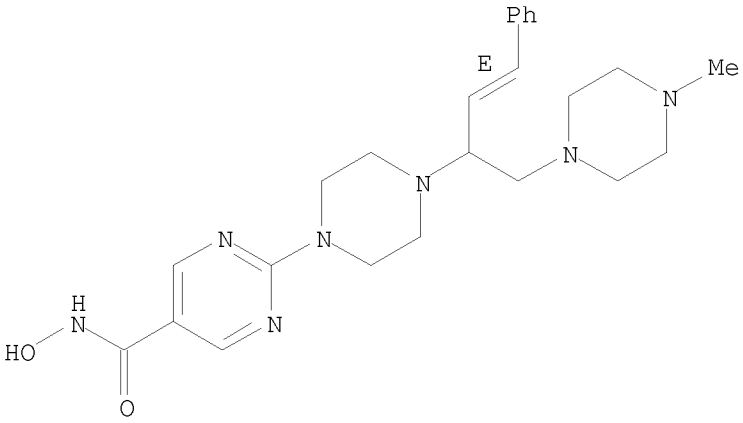


RN 875139-20-1 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(4-morpholinylmethyl)-3-phenyl-2-propen-1-yl]-1-piperazinyl]- (CA INDEX NAME)



RN 875139-21-2 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(2E)-1-[(4-methyl-1-piperazinyl)methyl]-3-phenyl-2-propen-1-yl]-1-piperazinyl]- (CA INDEX NAME)

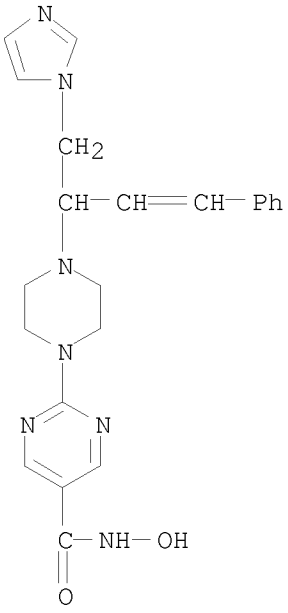
Double bond geometry as shown.



RN 875139-23-4 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(1H-imidazol-1-ylmethyl)-3-phenyl-2-propen-1-yl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

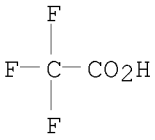
CM 1

CRN 875139-22-3
CMF C22 H25 N7 O2

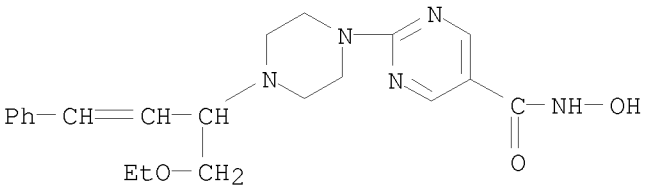


CM 2

CRN 76-05-1
CMF C2 H F3 O2



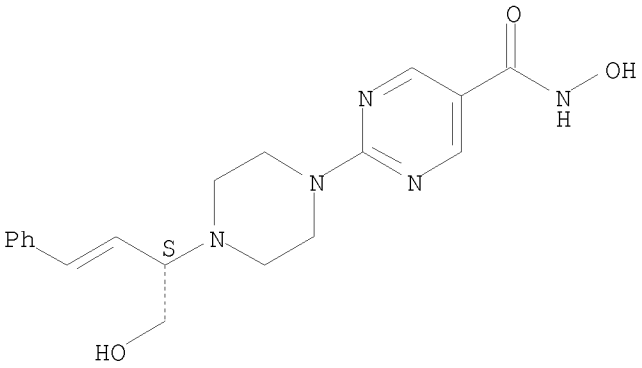
RN 875139-24-5 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-(ethoxymethyl)-3-phenyl-2-propen-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



RN 875139-25-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(1S)-1-(hydroxymethyl)-3-phenyl-2-propen-1-yl]-1-piperazinyl]- (CA INDEX NAME)

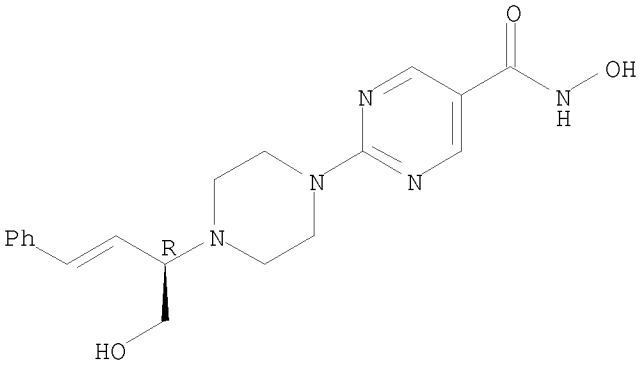
Absolute stereochemistry.

Double bond geometry unknown.



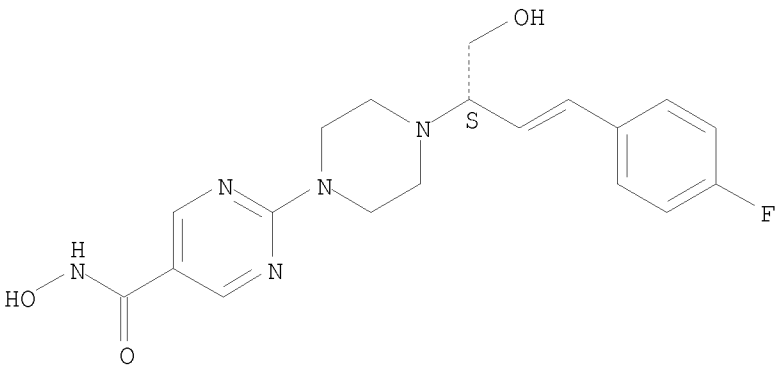
RN 875139-26-7 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(1R)-1-(hydroxymethyl)-3-phenyl-2-propen-1-yl]-1-piperazinyl]- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

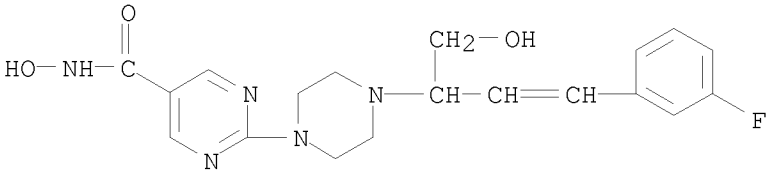


RN 875139-27-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(1S)-3-(4-fluorophenyl)-1-(hydroxymethyl)-2-propen-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)

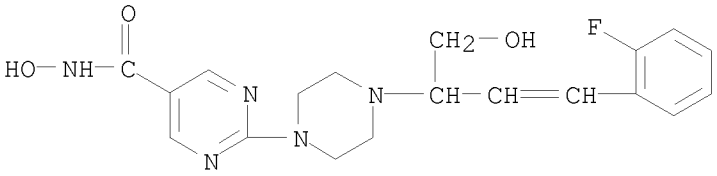
Absolute stereochemistry.
Double bond geometry unknown.



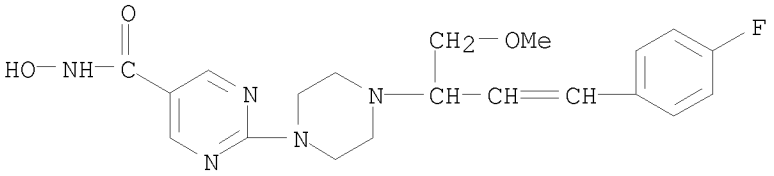
RN 875139-28-9 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3-(3-fluorophenyl)-1-(hydroxymethyl)-2-propen-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



RN 875139-29-0 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3-(2-fluorophenyl)-1-(hydroxymethyl)-2-propen-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



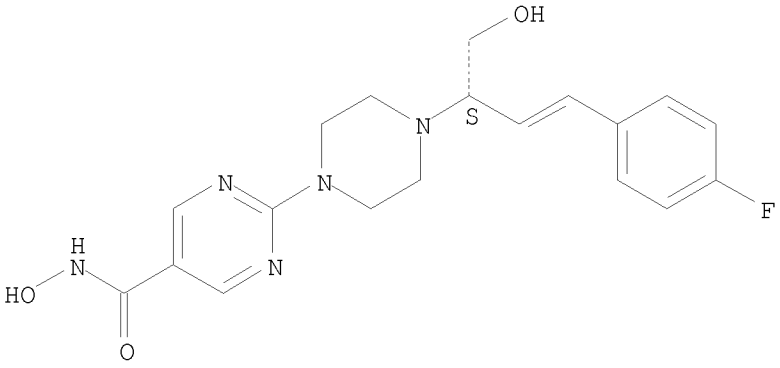
RN 875139-30-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3-(4-fluorophenyl)-1-(methoxymethyl)-2-propen-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



RN 875139-31-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(1S)-3-(4-fluorophenyl)-1-(hydroxymethyl)-2-

propen-1-yl]-1-piperazinyl]-N-hydroxy-, hydrochloride (1:1) (CA INDEX NAME)

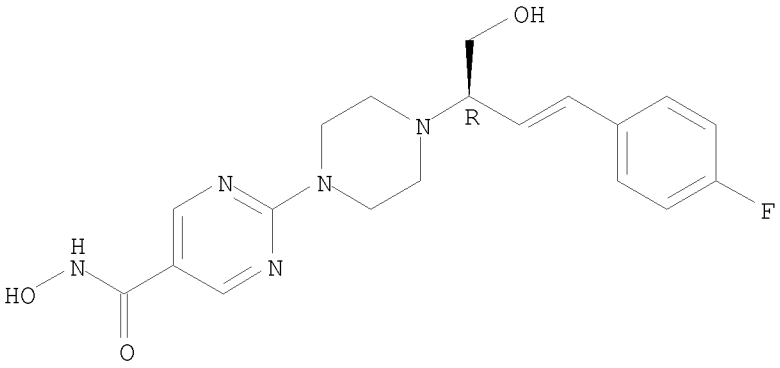
Absolute stereochemistry.
Double bond geometry unknown.



● HCl

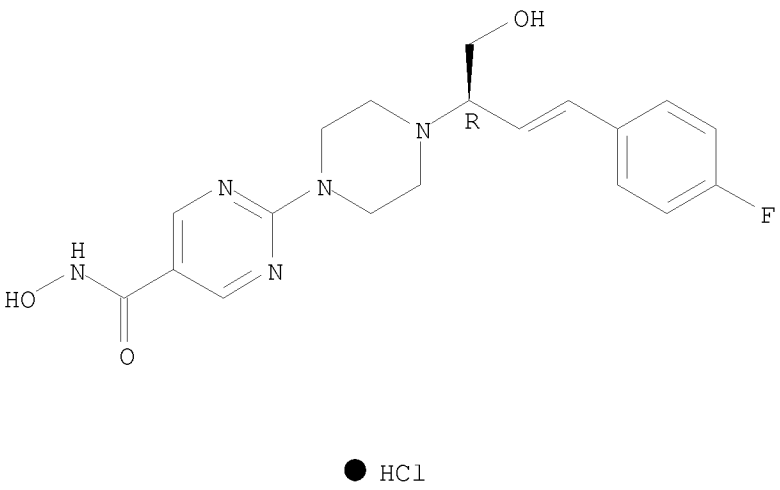
RN 875139-69-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(1R)-3-(4-fluorophenyl)-1-(hydroxymethyl)-2-propen-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 875139-70-1 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(1R)-3-(4-fluorophenyl)-1-(hydroxymethyl)-2-propen-1-yl]-1-piperazinyl]-N-hydroxy-, hydrochloride (1:1) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



● HCl

L11 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:300395 CAPLUS
DOCUMENT NUMBER: 142:355054
TITLE: Preparation of amide derivatives as inhibitors of histone deacetylase
INVENTOR(S): Moradei, Oscar; Paquin, Isabelle; Leit, Silvana; Frechette, Sylvie; Vaisburg, Arkadii; Besterman, Jeffrey M.; Tessier, Pierre; Mallais, Tammy C.
PATENT ASSIGNEE(S): Methylgene, Inc., Can.
SOURCE: PCT Int. Appl., 559 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2005030705	A1	20050407	WO 2004-US31591		20040924
WO 2005030705	A9	20060420			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2004276337	A1	20050407	AU 2004-276337		20040924
CA 2539117	A1	20050407	CA 2004-2539117		20040924
EP 1663953	A1	20060607	EP 2004-789074		20040924
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR					
CN 1882529	A	20061220	CN 2004-80034571		20040924
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PRIORITY APPLN. INFO.:			US 2003-505884P	P	20030924
			US 2003-532973P	P	20031229
			US 2004-561082P	P	20040409
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			WO 2004-US31591	W	20040924

OTHER SOURCE(S): CASREACT 142:355054; MARPAT 142:355054
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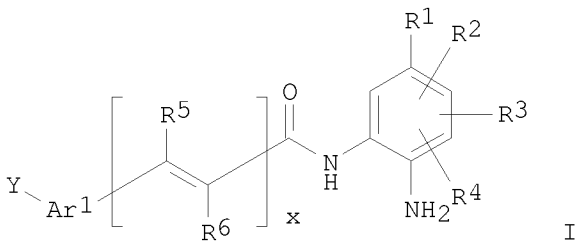

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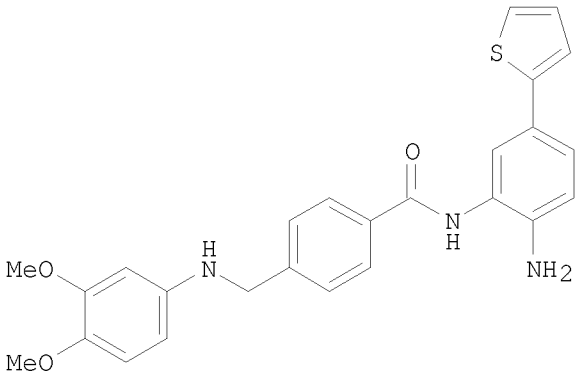
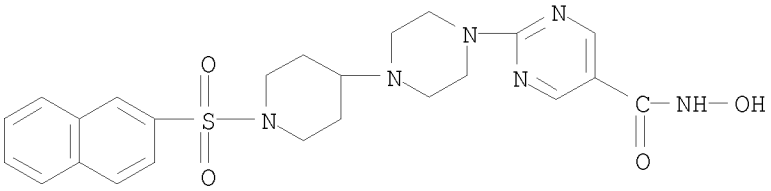


II

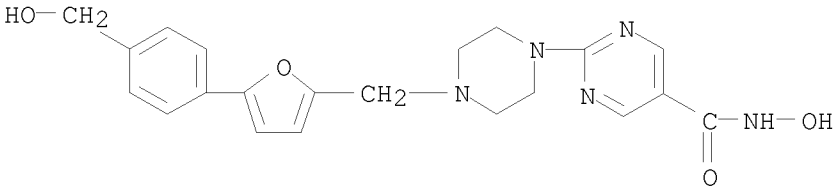
AB Title compds. I [Ar1 = (un)saturated-, (un)substituted-mono or fused poly-cyclic hydrocarbyl optionally containing 1-4 heteroatoms per ring; R1 = (un)substituted-mono-, -bi-, -tri-cyclic-aryl or -heteroaryl; R2, R3, and R4 independently = H, halo, amino, etc.; R5 and R6 independently = H, alkyl, aryl, etc.; x = 0-1; Y = any pharmaceutically acceptable chemical moiety consisting of 1 to 50 atoms with provisions] and their pharmaceutically acceptable salts, are prepared and disclosed as inhibitors of histone deacetylase. Thus, e.g., II was prepared by Suzuki coupling of 2-bromo-2-nitro-phenylamine (preparation given) with 2-thiopheneboronic acid followed by carbonylation with 4-[3,4-dimethoxy-(phenylamino)-methyl]benzoic acid (preparation given) and subsequent reduction The inhibitory capability of I towards antiproliferative activity of histone deacetylase enzyme was evaluated using 3-[4,5-dimethylthiazol-2-yl-2,5-diphenyltetrazolium] bromide (MTT) assay and it revealed that certain compds. of the invention had MTT IC 50 values in the range of below 1 up to 20 μM. I as histone deacetylase inhibitors should prove useful in the treatment of diseases such as, but not limited to, cell proliferative disease, protozoal disease, and fungal disease.

IT 603985-82-6P 603985-86-0P 603985-88-2P
603985-90-6P 603985-94-0P 603991-95-3P
603991-96-4P 603992-24-1P 603992-25-2P
603992-26-3P 603992-27-4P 603992-28-5P
604784-81-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amide derivs. as inhibitors of histone deacetylase)

RN 603985-82-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(2-naphthalenylsulfonyl)-4-piperidinyl]-1-piperazinyl]- (CA INDEX NAME)



RN 603985-86-0 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[5-[4-(hydroxymethyl)phenyl]-2-furanyl]methyl]-1-piperazinyl]- (CA INDEX NAME)



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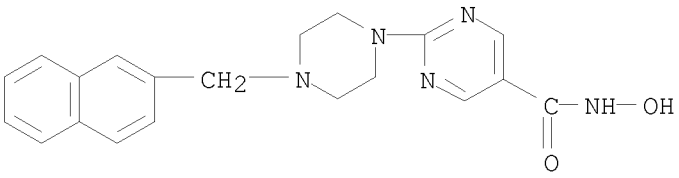

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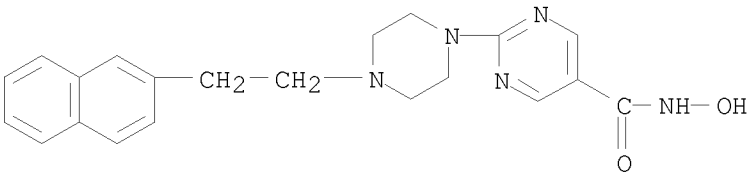

RN 603985-94-0 CAPLUS
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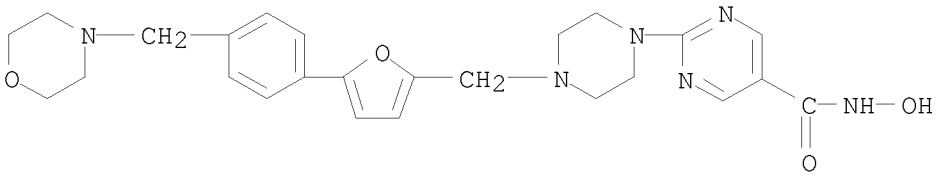
NAME)



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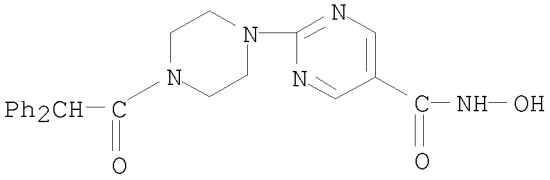

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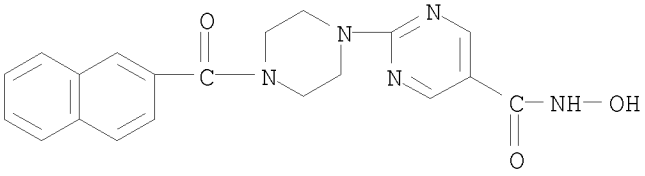

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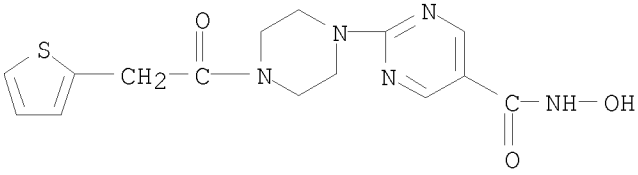

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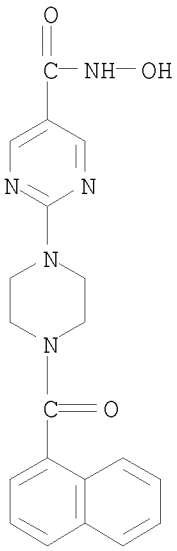

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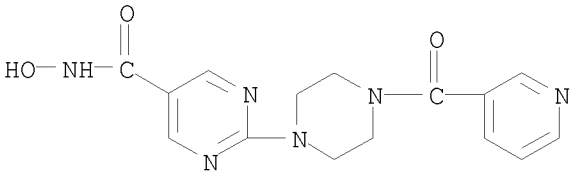

RN 603992-27-4 CAPLUS
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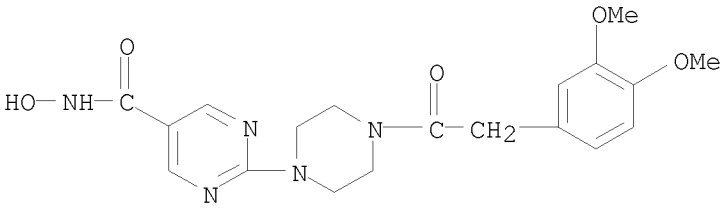

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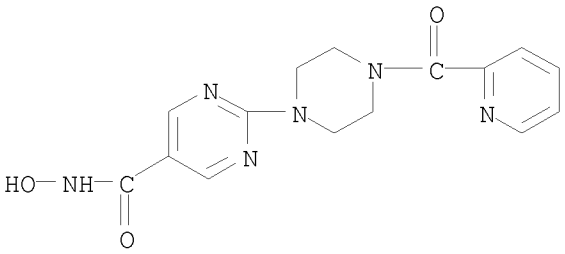

RN 604784-81-8 CAPLUS
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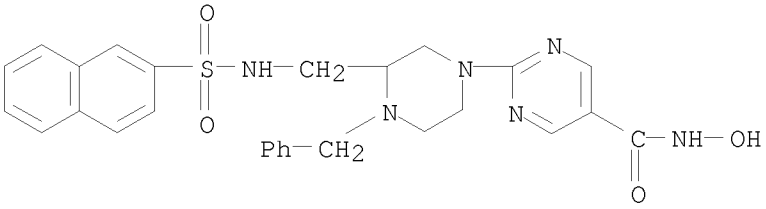

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:300394 CAPLUS
DOCUMENT NUMBER: 142:373563
TITLE: Preparation of amide derivatives as inhibitors of histone deacetylase
INVENTOR(S): Moradei, Oscar; Paquin, Isabelle; Leit, Silvana; Frechette, Sylvie; Vaisburg, Arkadii; Besterman, Jeffrey M.; Tessier, Pierre; Mallais, Tammy C.
PATENT ASSIGNEE(S): Methylgene, Inc., Can.
SOURCE: PCT Int. Appl., 389 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005030704	A1	20050407	WO 2004-US31590	20040924
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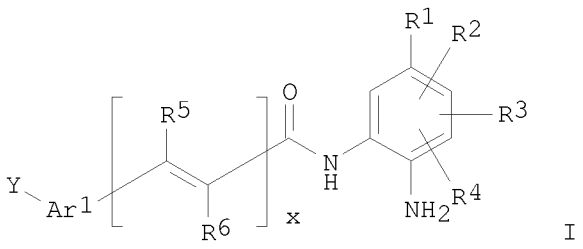
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
JP 2008094847	A	20080424	JP 2007-281356	20071030

PRIORITY APPLN. INFO.:
US 2003-505884P P 20030924
US 2003-532973P P 20031229
US 2004-561082P P 20040409
JP 2006-528279 A3 20040924

OTHER SOURCE(S): CASREACT 142:373563; MARPAT 142:373563
GI



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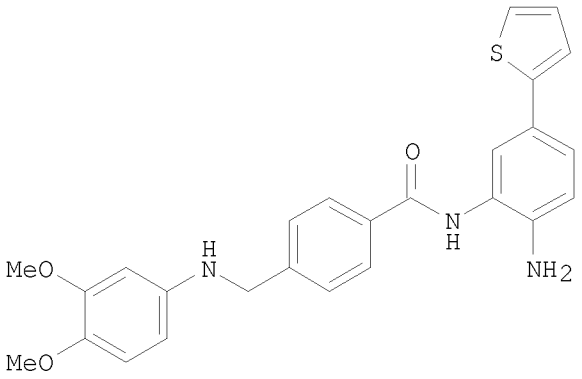
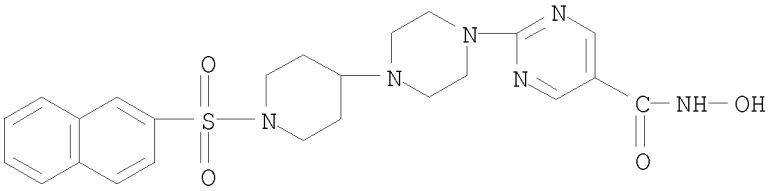


II

AB Title compds. I [Ar1 = (un)saturated-, (un)substituted-mono or fused poly-cyclic hydrocarbyl optionally containing 1-4 heteroatoms per ring; R1 = (un)substituted-mono-, -bi-, -tri-cyclic-aryl or -heteroaryl; R2, R3, and R4 independently = H, halo, amino, etc.; R5 and R6 independently = H, alkyl, aryl, etc.; x = 0-1; Y = any pharmaceutically acceptable chemical moiety consisting of 1 to 50 atoms with provisions] and their pharmaceutically acceptable salts, are prepared and disclosed as inhibitors of histone deacetylase. Thus, e.g., II was prepared by Suzuki coupling of 2-bromo-2-nitro-phenylamine (preparation given) with 2-thiopheneboronic acid followed by carbonylation with 4-[3,4-dimethoxy-(phenylamino)-methyl]benzoic acid (preparation given) and subsequent reduction The inhibitory capability of I towards antiproliferative activity of histone deacetylase enzyme was evaluated using 3-[4,5-dimethylthiazol-2-yl-2,5-diphenyltetrazolium] bromide (MTT) assay and it revealed that certain compds. of the invention had MTT IC 50 values in the range of below 1 up to 20 μM. I as histone deacetylase inhibitors should prove useful in the treatment of diseases such as, but not limited to, cell proliferative disease, protozoal disease, and fungal disease.

IT 603985-82-6P 603985-86-0P 603985-88-2P
603985-90-6P 603985-94-0P 603991-95-3P
603991-96-4P 603992-24-1P 603992-25-2P
603992-26-3P 603992-27-4P 603992-28-5P
604784-81-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amide derivs. as inhibitors of histone deacetylase)

RN 603985-82-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(2-naphthalenylsulfonyl)-4-piperidinyl]-1-piperazinyl]- (CA INDEX NAME)



RN 603985-86-0 CAPLUS
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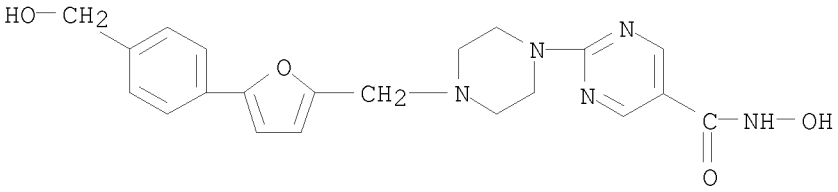

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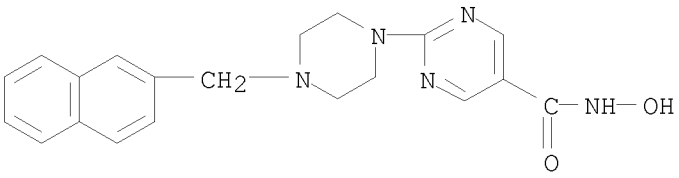
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-naphthalenylmethyl)-1-piperazinyl]- (CA INDEX NAME)



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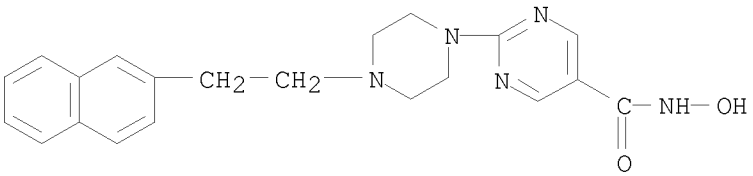
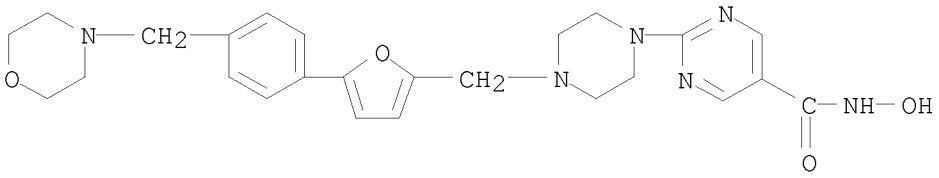


RN 603985-94-0 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[5-[4-(4-morpholinylmethyl)phenyl]-2-furanyl]methyl]-1-piperazinyl]- (CA INDEX

NAME)



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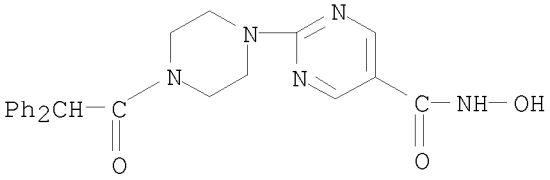
CN 5-Pyrimidinecarboxamide, 2-[4-(2,2-diphenylacetyl)-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



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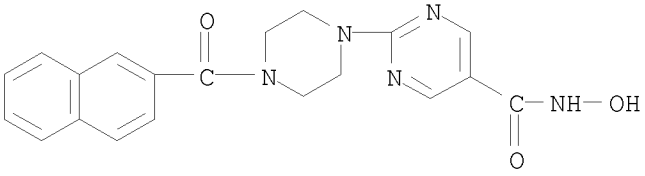

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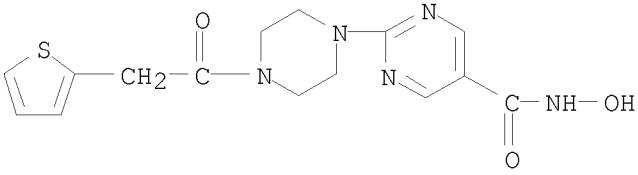

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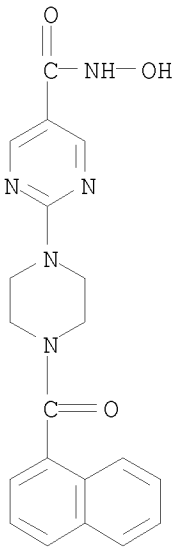

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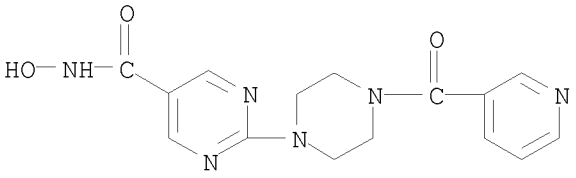
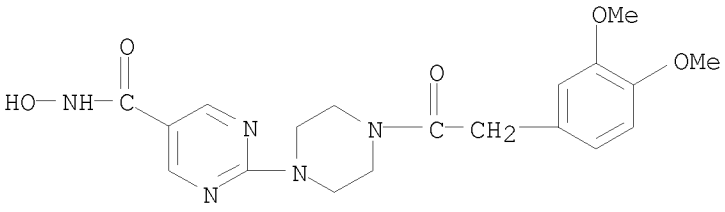


RN 603992-27-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[2-(3,4-dimethoxyphenyl)acetyl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



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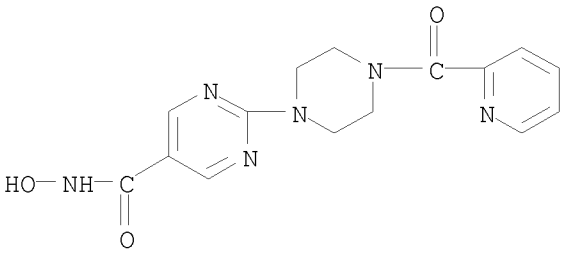
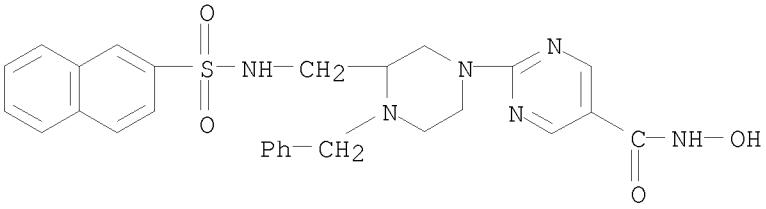


RN 604784-81-8 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[3-[[(2-naphthalenylsulfonyl)amino]methyl]-4-(phenylmethyl)-1-piperazinyl]- (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:737757 CAPLUS
DOCUMENT NUMBER: 139:276911
TITLE: Preparation of N-(piperazinylmethyl-, piperidinylmethyl- and morpholinylmethyl) sulfonamides and amides as novel inhibitors of histone deacetylase
INVENTOR(S): Van Emelen, Kristof
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076438	A1	20030918	WO 2003-EP2510	20030311
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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AU 2003218735	A1	20030922	AU 2003-218735	20030311
EP 1485378	A1	20041215	EP 2003-711979	20030311
EP 1485378	B1	20080618		
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BR 2003007606	A	20041221	BR 2003-7606	20030311
CN 1642948	A	20050720	CN 2003-805921	20030311
JP 2005526766	T	20050908	JP 2003-574655	20030311
NZ 534833	A	20060728	NZ 2003-534833	20030311
CN 101007803	A	20070801	CN 2007-10005212	20030311
AT 398615	T	20080715	AT 2003-711979	20030311
TW 283676	B	20070711	TW 2003-92105285	20030312
IN 2004DN02536	A	20070413	IN 2004-DN2536	20040831
US 20050165016	A1	20050728	US 2004-507084	20040908
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NO 2004004135	A	20040929	NO 2004-4135	20040929
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			WO 2002-EP14833	A 20021223
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			WO 2003-EP2510	W 20030311

OTHER SOURCE(S): MARPAT 139:276911
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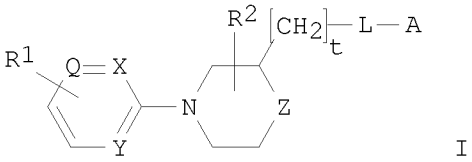

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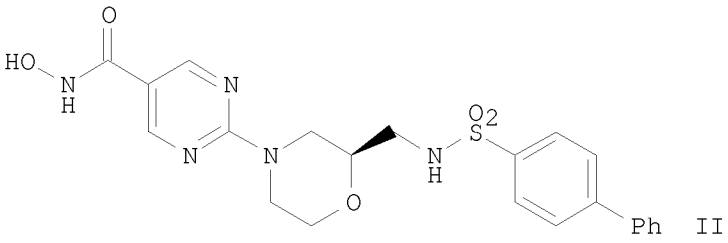


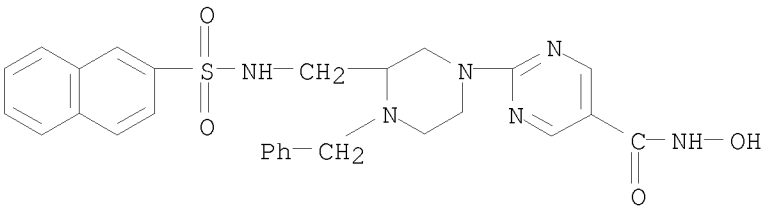
II

AB The title compds. [I; t = 0-4; Q, X, Y = N, C; Z = NH, O, CH2; R1 = CONR3R4, NHCOR7, CO(alkanediyl)SR7, etc. (wherein R3, R4 = H, OH, alkyl, etc.; R7 = H, alkyl, alkylcarbonyl, etc.); R2 = H, OH, NH2, etc.; L = NR9CO, NR9SO2, NR9CH2 (R9 = H, alkyl, cycloalkyl, etc.); A = (un)substituted Ph, cycloalkyl, pyridyl, etc.], having histone deacetylase inhibiting enzymic activity, were prepared and formulated. E.g., a multi-step synthesis of (+)-II which showed pIC50 of 7.723 against HDAC, was given.

IT 604784-81-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-(piperazinylmethyl-, piperidinylmethyl- and morpholinylmethyl) sulfonamides and amides as novel inhibitors of histone deacetylase)

RN 604784-81-8 CAPLUS

CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[3-[[(2-naphthalenylsulfonyl)amino]methyl]-4-(phenylmethyl)-1-piperazinyl]- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

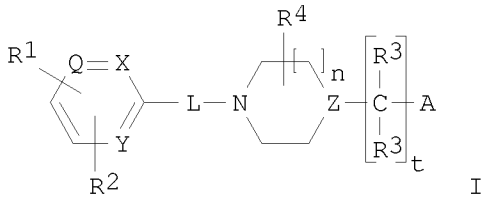
L11 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:737723 CAPLUS
DOCUMENT NUMBER: 139:261309
TITLE: Preparation of N-hydroxy-5-piperazino(piperidino or diazepino)-2-pyrimidinecarboxamides and N-hydroxy-4-piperazino(piperidino or diazepino)benzamides as new inhibitors of histone deacetylase
INVENTOR(S): Angibaud, Patrick Rene; Pilatte, Isabelle Noeelle Constance; Van Brandt, Sven Franciscus Anna; Roux, Bruno; Ten Holte, Peter; Verdonck, Marc Gustaaf Celine; Meerpoel, Lieven; Dyatkin, Alexey Borisovich
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076400	A1	20030918	WO 2003-EP2514	20030311
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2475764	A1	20030918	CA 2003-2475764	20030311
AU 2003218736	A1	20030922	AU 2003-218736	20030311
EP 1485353	A1	20041215	EP 2003-711980	20030311
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003008081	A	20041221	BR 2003-8081	20030311
CN 1639125	A	20050713	CN 2003-805675	20030311
CN 1642551	A	20050720	CN 2003-805833	20030311
NZ 534834	A	20050729	NZ 2003-534834	20030311
JP 2005526067	T	20050902	JP 2003-574621	20030311
CN 101007803	A	20070801	CN 2007-10005212	20030311
IN 2004DN02533	A	20070413	IN 2004-DN2533	20040831
US 20050107384	A1	20050519	US 2004-506998	20040908
ZA 2004007237	A	20050928	ZA 2004-7237	20040909
ZA 2004007235	A	20051004	ZA 2004-7235	20040909
ZA 2004007232	A	20051006	ZA 2004-7232	20040909
ZA 2004007233	A	20051006	ZA 2004-7233	20040909
ZA 2004007234	A	20051006	ZA 2004-7234	20040909
ZA 2004007236	A	20051006	ZA 2004-7236	20040909
MX 2004PA08806	A	20041126	MX 2004-PA8806	20040910
NO 2004004194	A	20041001	NO 2004-4194	20041001
PRIORITY APPLN. INFO.:			US 2002-363799P	P 20020313
			WO 2002-EP14833	A 20021223
			CN 2003-805921	A3 20030311

WO 2003-EP2514 W 20030311

OTHER SOURCE(S): MARPAT 139:261309

GI



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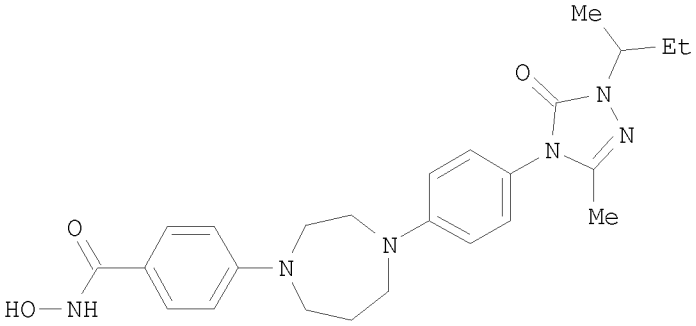

II

AB The title compds. [I; n = 0-3; t = 0-4; Q, X, Y = N, C; Z = N, CH; R1 = CONR7R8, NHCOR9, CO(alkanediyl)SR9, etc. (wherein R7, R8 = H, OH, alkyl, etc.; R9 = H, alkyl, alkylcarbonyl, etc.); R2 = H, halo, OH, etc.; L = a bond, alkanediyl, alkanediyloxy, NH, CO, NHCO; each R3 = H and one H atom can be replaced by aryl; R4 = H, OH, NH2, etc.; A = (un)substituted Ph, cyclohexyl, pyridyl, etc.], having histone deacetylase inhibiting enzymic activity, were prepared and formulated. E.g., a multi-step synthesis of II which showed pIC50 of 5.121 against HDAC, was given.

IT 603985-83-7P 603985-87-1P 603985-89-3P
603985-91-7P 603985-95-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazino(piperidino or diazepino) substituted 2-pyrimidinecarbohydroxamic acids and N-hydroxybenzamides as new inhibitors of histone deacetylase)

RN 603985-83-7 CAPLUS

CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(2-naphthalenylsulfonyl)-4-piperidinyl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (10:9) (CA INDEX NAME)

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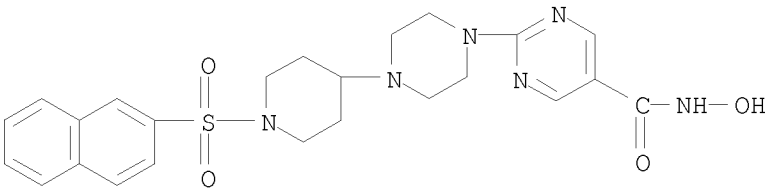
CRN 603985-82-6
CMF C24 H28 N6 O4 S



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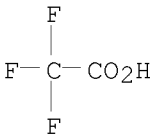
CRN 76-05-1
CMF C2 H F3 O2



RN 603985-87-1 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[5-[4-(hydroxymethyl)phenyl]-2-furanyl]methyl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (5:4) (CA INDEX NAME)

CM 1

CRN 603985-86-0
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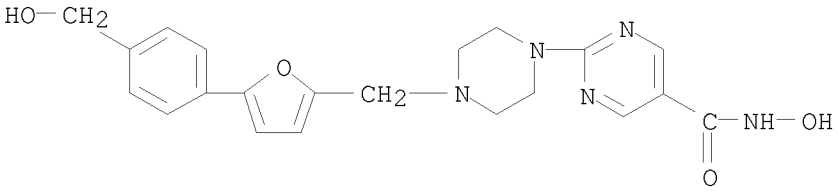

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CRN 76-05-1
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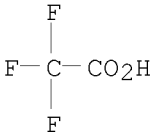

RN 603985-89-3 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-naphthalenylmethyl)-1-piperazinyl]-, 2,2,2-trifluoroacetate (5:4) (CA INDEX NAME)

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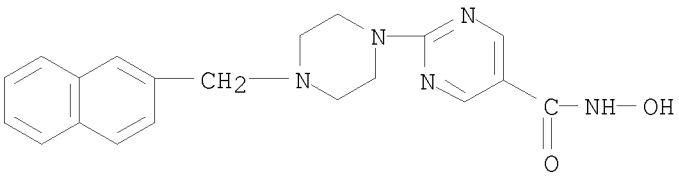
CRN 603985-88-2
CMF C20 H21 N5 O2



CM 2

CRN 76-05-1
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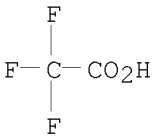

RN 603985-91-7 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[2-(2-naphthalenyl)ethyl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (5:4) (CA INDEX NAME)

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CRN 603985-90-6
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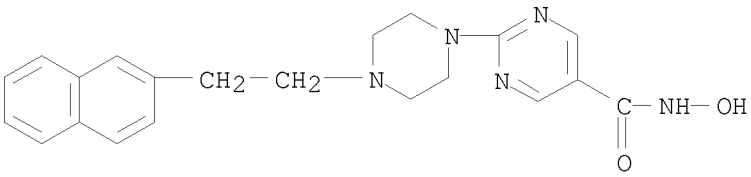
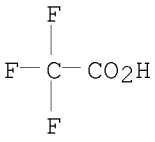


CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 603985-95-1 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[5-[4-(4-morpholinylmethyl)phenyl]-2-furanyl]methyl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:2) (CA INDEX NAME)

CM 1

CRN 603985-94-0
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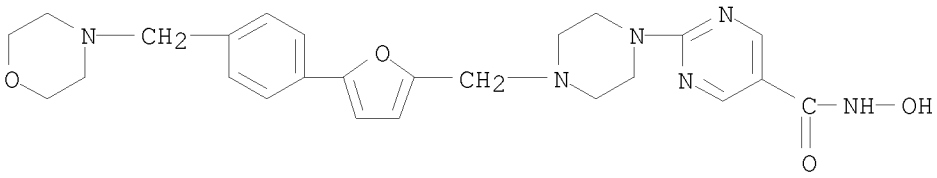
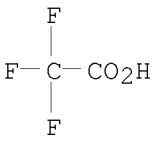


CM 2

CRN 76-05-1
CMF C2 H F3 O2



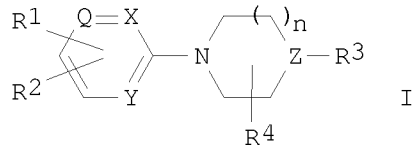
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:737586 CAPLUS
DOCUMENT NUMBER: 139:261308
TITLE: Preparation of aryl and heteroaryl hydroxamic acids as inhibitors of histone deacetylase for treating proliferative diseases
INVENTOR(S): Van Emelen, Kristof; Verdonck, Marc Gustaaf Celine; Van Brandt, Sven Franciscus Anna; Angibaud, Patrick Rene; Meerpoel, Lieven; Dyatkin, Alexey Borisovich
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003075929	A1	20030918	WO 2003-EP2515		20030311
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2476065	A1	20030918	CA 2003-2476065		20030311
AU 2003218737	A1	20030922	AU 2003-218737		20030311
AU 2003218737	B2	20080410			
EP 1485099	A1	20041215	EP 2003-711981		20030311
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003007624	A	20050111	BR 2003-7624		20030311
CN 1639125	A	20050713	CN 2003-805675		20030311
CN 1642551	A	20050720	CN 2003-805833		20030311
JP 2005525379	T	20050825	JP 2003-574203		20030311
NZ 534832	A	20050930	NZ 2003-534832		20030311
CN 101007803	A	20070801	CN 2007-10005212		20030311
IN 2004DN02537	A	20070112	IN 2004-DN2537		20040831
ZA 2004007237	A	20050928	ZA 2004-7237		20040909
ZA 2004007235	A	20051004	ZA 2004-7235		20040909
ZA 2004007232	A	20051006	ZA 2004-7232		20040909
ZA 2004007233	A	20051006	ZA 2004-7233		20040909
ZA 2004007234	A	20051006	ZA 2004-7234		20040909
ZA 2004007236	A	20051006	ZA 2004-7236		20040909
MX 2004PA08797	A	20041126	MX 2004-PA8797		20040910
US 20050096468	A1	20050505	US 2004-507785		20040913
NO 2004004113	A	20040928	NO 2004-4113		20040928
PRIORITY APPLN. INFO.:			US 2002-363799P	P	20020313
			WO 2002-EP14833	A	20021223
			CN 2003-805921	A3	20030311
			WO 2003-EP2515	W	20030311

OTHER SOURCE(S): MARPAT 139:261308

GI



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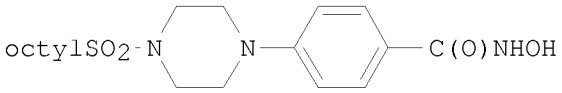


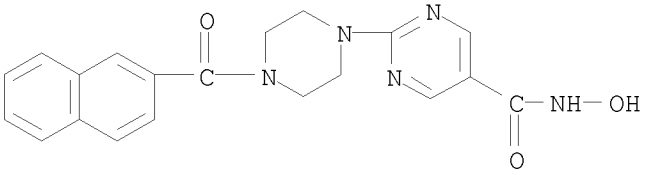
II

AB This invention comprises aryl and heteroaryl hydroxamic acids (shown as I; variables defined below; e.g. II) having histone deacetylase inhibiting enzymic activity; their preparation, compns. containing them and their use as a medicine. Compds. I show excellent in-vitro histone deacetylase inhibiting enzymic activity, have advantageous properties with regard to cellular activity and specific properties with regard to inhibition of cell cycle progression at both G1 and G2 checkpoints (p21 induction capacity), and show good metabolic stability and high bioavailability and more particular show oral bioavailability. They can also be used for detection and identification of histone deacetylase. General synthetic procedures and characterization data for twenty-seven I are included; also, prepns. of 12 intermediates are included. For example, a 59 % yield of 2-[4-(dimethylaminosulfonyl)piperazin-1-yl]pyrimidine-5-carbohydroxamic acid was obtained by removing the O-tetrahydropyranyl group of its ester using trifluoroacetic acid; the ester was prepared in 61 % yield from N'-(ethylcarbonimidoyl)-N,N-dimethyl-1,3-propanediamine monohydrochloride, sodium 2-[4-(dimethylaminosulfonyl)piperazin-1-yl]pyrimidine-5-carboxylate, O-(tetrahydro-2H-pyran-2-yl)hydroxylamine, and 1-hydroxy-1H-benzotriazole in CH2Cl2/THF. The sodium salt was obtained by base hydrolysis of the Et ester; the ester was prepared in 73 % yield from Et 2-(piperazin-1-yl)pyrimidine-5-carboxylate and dimethylsulfamoyl chloride; Et 2-(piperazin-1-yl)pyrimidine-5-carboxylate was obtained in <96 % yield from Et 2-(4-benzylpiperazin-1-yl)pyrimidine-5-carboxylate by hydrogenation using Pd/C; the benzyl derivative was obtained from 1-(phenylmethyl)piperazine, (135 mL) was added gradually to a solution of potassium carbonate (0.18 mol) and 2-(methylsulfonyl)-5-pyrimidinecarboxylic acid Et ester, K2CO3 in MeCN. For I: n is 0-3; Q, X and Y are N or C; Z is N or CH; R1 is -C(O)NR5R6, -N(H)C(O)R7, -C(O)-C1-6alkanediylSR7, -NR8C(O)N(OH)R7, -NR8C(O)C1-6alkanediylSR7, -NR8C(O)C:N(OH)R7 or another Zn-chelating-group; R2 is H, halo, hydroxy, amino, nitro, C1-6alkyl, C1-6alkyloxy, trifluoromethyl, di(C1-6-alkyl)amino, hydroxyamino or naphthalenylsulfonylpyrazinyl. R3 is H, C1-6-alkyl, arylC2-6alkenediyl, furanylcarbonyl, naphthalenylcarbonyl, -C(O)phenylR9, C1-6alkylaminocarbonyl, aminosulfonyl, arylaminosulfonyl, aminosulfonylamino, di(C1-6-alkyl)aminosulfonylamino, arylaminosulfonylamino, aminosulfonylaminoC1-6-alkyl, di(C1-6-alkyl)aminosulfonylaminoC1-6-alkyl, arylaminosulfonylaminoC1-6alkyl, di(C1-6-alkyl)aminoC1-6alkyl, Cl1-12-alkylsulfonyl, di(C1-6-alkyl)aminosulfonyl, trihaloC1-6-alkylsulfonyl, di(aryl)C1-6alkylcarbonyl, thiophenylC1-6alkylcarbonyl, pyridinylcarbonyl or arylC1-6alkylcarbonyl. R4 is H, hydroxy, amino, hydroxyC1-6alkyl, C1-6alkyl, C1-6alkyloxy,

arylC1-6alkyl, aminocarbonyl, hydroxycarbonyl, aminoC1-6-alkyl, aminocarbonylC1-6-alkyl, hydroxycarbonylC1-6-alkyl, hydroxyaminocarbonyl, C1-6-alkyloxycarbonyl, C1-6-alkylaminoC1-6-alkyl or di(C1-6-alkyl)aminoC1-6-alkyl; when R3 and R4 are present on the same C atom, R3 and R4 together may form -C(O)-NH-CH2-NR10- wherein R10 is H or aryl; when R3 and R4 are present on adjacent C atoms, R3 and R4 together may form :CH-CH:CH-CH: ; addnl. details are given in the claims.

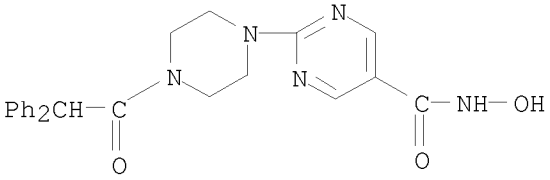
IT 603991-96-4P
RL: ARG (Analytical reagent use); PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate and reagent for detection/identification of histone deacetylase; preparation of aryl and heteroaryl hydroxamic acids as inhibitors of histone deacetylase for treating proliferative diseases)

RN 603991-96-4 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-naphthalenylcarbonyl)-1-piperazinyl]- (CA INDEX NAME)



IT 603991-95-3P 603992-24-1P 603992-25-2P
603992-26-3P 603992-27-4P 603992-28-5P
RL: ARG (Analytical reagent use); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate and reagent for detection/identification of histone deacetylase; preparation of aryl and heteroaryl hydroxamic acids as inhibitors of histone deacetylase for treating proliferative diseases)

RN 603991-95-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-(2,2-diphenylacetyl)-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



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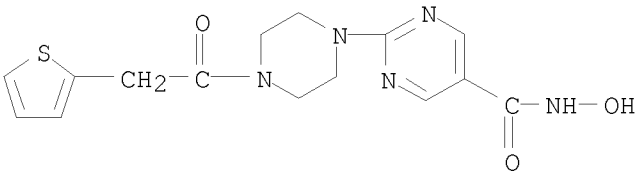

RN 603992-25-2 CAPLUS
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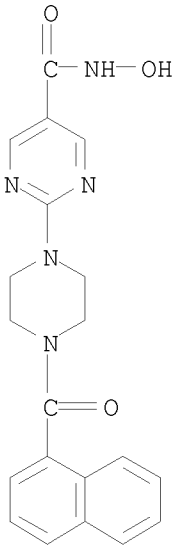
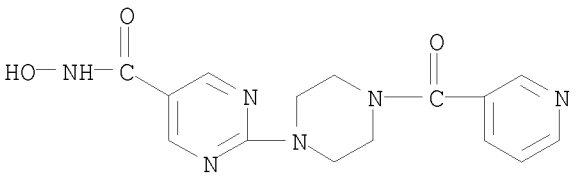


RN 603992-26-3 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(3-pyridinylcarbonyl)-1-piperazinyl]- (CA INDEX NAME)



RN 603992-27-4 CAPLUS
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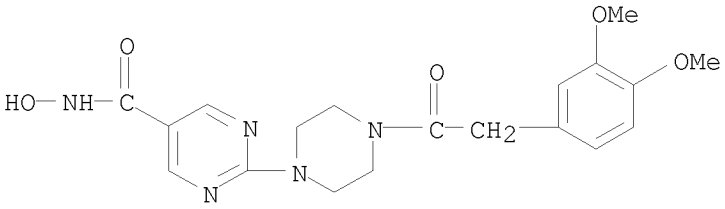
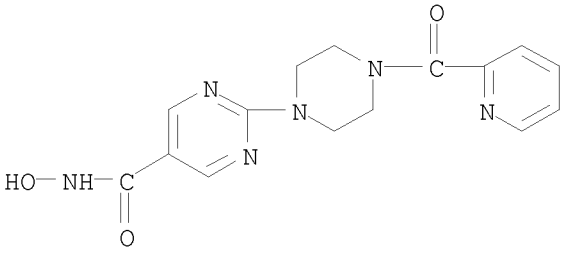


RN 603992-28-5 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-pyridinylcarbonyl)-1-piperazinyl]- (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> file erg
'ERG' IS NOT A VALID FILE NAME
SESSION CONTINUES IN FILE 'CAPLUS'
Enter "HELP FILE NAMES" at an arrow prompt (=>) for a list of files
that are available.  If you have requested multiple files, you can
specify a corrected file name or you can enter "IGNORE" to continue
accessing the remaining file names entered.

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                      71.33     671.99

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                     -10.40     -19.20

FILE 'REGISTRY' ENTERED AT 16:08:09 ON 15 SEP 2008
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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provided by InfoChem.

STRUCTURE FILE UPDATES:   14 SEP 2008  HIGHEST RN 1049627-95-3
DICTIONARY FILE UPDATES:  14 SEP 2008  HIGHEST RN 1049627-95-3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH July 5, 2008.

  Please note that search-term pricing does apply when
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on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

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Uploading C:\Program Files\Stnexp\Queries\10506998five.str
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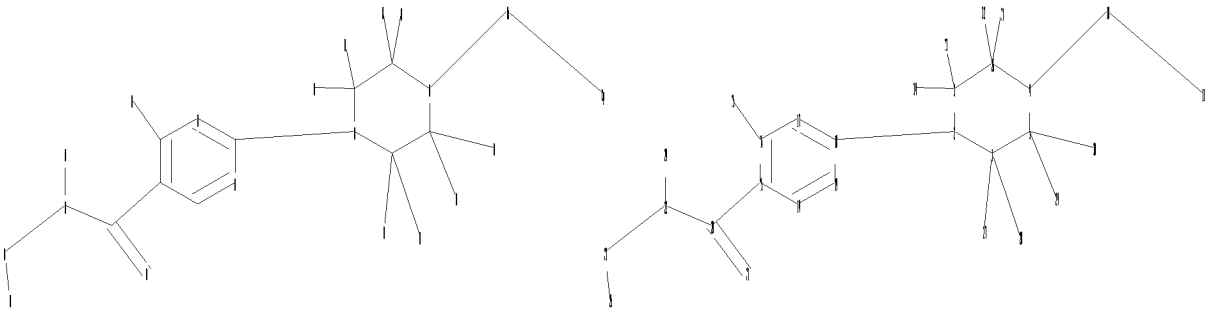


chain nodes :
10 11 20 21 22 23 24 25 27 28 29 30 31 32 33 34 35
ring nodes :
1 2 3 4 5 14 15 16 17 18 19 26
chain bonds :
1-27 1-28 2-18 3-33 3-34 4-10 5-29 5-30 10-11 15-20 16-35 20-21 20-22
22-23 22-24 23-25 26-31 26-32
ring bonds :
1-2 1-5 2-3 3-26 4-5 4-26 14-15 14-19 15-16 16-17 17-18 18-19
exact/norm bonds :
1-2 1-5 2-3 2-18 3-26 4-10 4-5 4-26 10-11 20-21 20-22 22-23
exact bonds :
1-27 1-28 3-33 3-34 5-29 5-30 15-20 16-35 22-24 23-25 26-31 26-32
normalized bonds :
14-15 14-19 15-16 16-17 17-18 18-19
isolated ring systems :
containing 1 :

G1:C,N

G2:Ak,NH2,NO2

G3:O

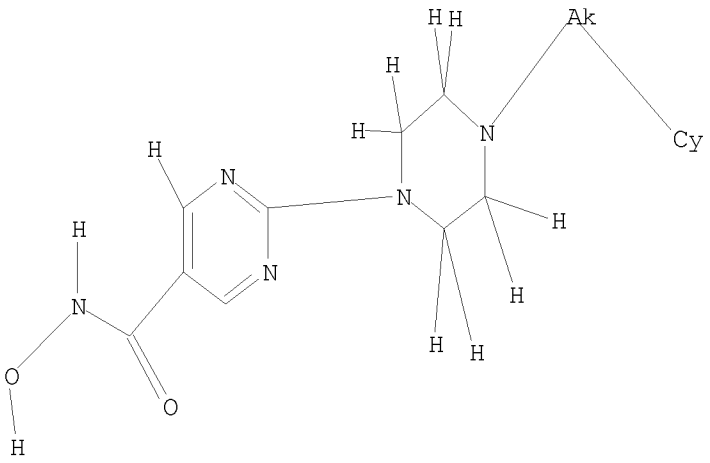
G4

G5:C,N,Zn,H

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 10:CLASS 11:Atom 14:Atom 15:Atom
16:Atom 17:Atom 18:Atom 19:Atom 20:CLASS 21:CLASS 22:CLASS 23:CLASS
24:CLASS 25:CLASS 26:Atom 27:CLASS 28:CLASS 29:CLASS 30:CLASS 31:CLASS
32:CLASS 33:CLASS 34:CLASS 35:CLASS

L12 STRUCTURE UPLOADED

=> d l12
L12 HAS NO ANSWERS
L12 STR



G1 C,N

G2 Ak,NH2,NO2

G3 O

G4

G5 C,N,Zn,H

Structure attributes must be viewed using STN Express query preparation.

=> s l12 full
FULL SEARCH INITIATED 16:08:56 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 1679 TO ITERATE

100.0% PROCESSED 1679 ITERATIONS 89 ANSWERS
SEARCH TIME: 00.00.01

L13 89 SEA SSS FUL L12

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	178.82	850.81

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-19.20

FILE 'CAPLUS' ENTERED AT 16:09:04 ON 15 SEP 2008

FILE COVERS 1907 - 15 Sep 2008 VOL 149 ISS 12
FILE LAST UPDATED: 14 Sep 2008 (20080914/ED)

Caplus now includes complete International Patent Classification (IPC)
reclassification data for the second quarter of 2008.

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/legal/infopolicy.html

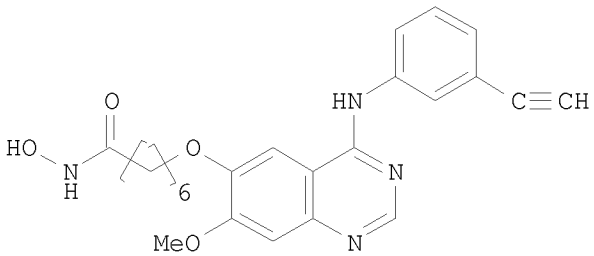
=> s l13 full
L14 9 L13

=> d ibib abs hitstr tot

L14 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:353001 CAPLUS
DOCUMENT NUMBER: 148:355828
TITLE: Multi-functional small molecules as anti-proliferative agents and their preparation
INVENTOR(S): Cai, Xiong; Qian, Changgeng; Gould, Stephen; Zhai, Haixiao
PATENT ASSIGNEE(S): Curis, Inc., USA
SOURCE: PCT Int. Appl., 494pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008033747	A2	20080320	WO 2007-US77971	20070910
WO 2008033747	A9	20080724		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
US 20080221132	A1	20080911	US 2007-852458	20070910
PRIORITY APPLN. INFO.:			US 2006-843590P P	20060911
			US 2007-895889P P	20070320

OTHER SOURCE(S): MARPAT 148:355828
GI



A—B—C I II

AB The invention relates to the compns., methods, and applications of an approach to selective inhibition of several cellular or mol. targets with a single small mol. More specifically, the present invention relates to multi-functional small mols. of formula I wherein one functionality is capable of inhibiting histone deacetylases (HDAC) and the other functionality is capable of inhibiting a different cellular or mol. pathway involved in aberrant cell proliferation, differentiation or

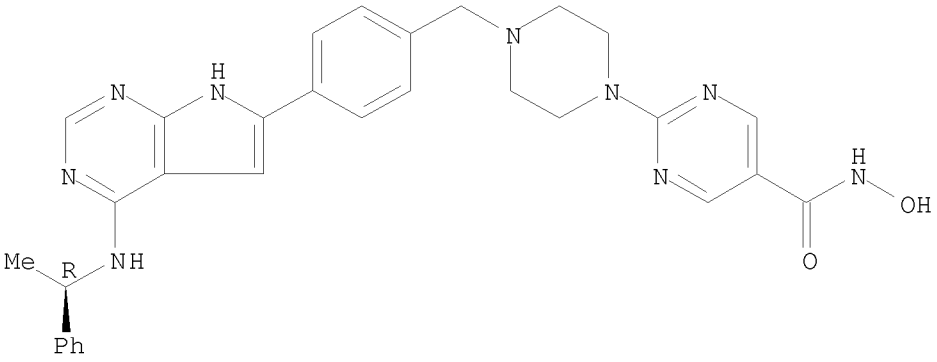
survival. Compds. of formula I wherein A is a pharmacophore of an anticancer agent capable of inhibiting at least one cellular or mol. pathway involved in the aberrant cell proliferation, differentiation or survival; B is a linker; C is a zinc-binding moiety; and their geometrical isomers, enantiomers, diastereoisomers, racemates, pharmaceutically acceptable salts, prodrugs and solvates thereof, are claimed. Example compound II was prepared by a multistep procedure (procedure given). All the invention compds. were evaluated for their antiproliferative activity (some data given).

IT 1011716-90-7P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRPH (Prophetic); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prophetic starting material; preparation of multi-functional small mols. as antiproliferative agents)

RN 1011716-90-7 CAPLUS

CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[4-[4-[[(1R)-1-phenylethyl]amino]-7H-pyrrolo[2,3-d]pyrimidin-6-yl]phenyl]methyl]-1-piperazinyl]- (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:351928 CAPLUS
DOCUMENT NUMBER: 148:355814
TITLE: Preparation of (aralkylamino)(phenyl)pyrrolo[2,3-d]pyrimidine derivatives for use as protein tyrosine kinase (PTK) inhibitors
INVENTOR(S): Cai, Xiong; Qian, Changgeng; Gould, Stephen
PATENT ASSIGNEE(S): Curis, Inc., USA
SOURCE: PCT Int. Appl., 123pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008033745	A2	20080320	WO 2007-US77968	20070910
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 20080161320	A1	20080703	US 2007-852440	20070910
PRIORITY APPLN. INFO.:			US 2006-843646P P	20060911
			US 2007-895894P P	20070320

OTHER SOURCE(S): MARPAT 148:355814
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

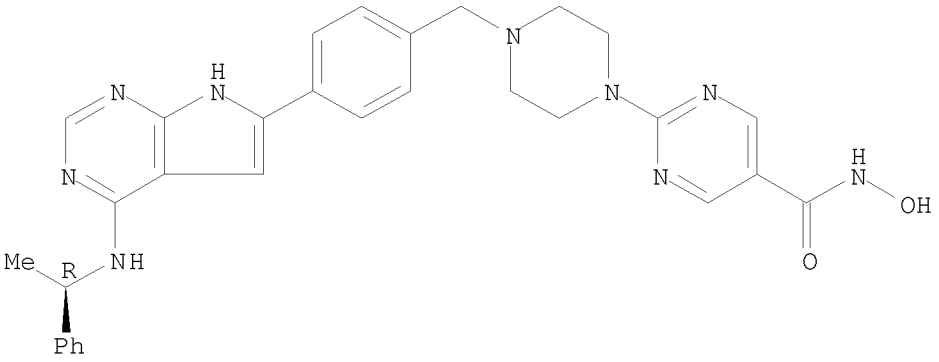
AB Fused bicyclic pyrimidine derivs. I and II [Ar = aryl, substituted arylheteroaryl or heteroaryl; Q = absent or (un)substituted alkyl; X = O, S, NH, or alkylamino; Z = O, S, NR1; Y = N or CR2; B = linker; D = C(O)NH2, NHC(S)CH3, CHC(O)NHacyl, etc.; R1 = H or (un)substituted alkyl; R2 = H, halo, (un)substituted aliphatic, aryl or heteroaryl], and their pharmaceutically acceptable salts, are prepared and disclosed as protein tyrosine kinase (PTK) inhibitors. Thus, e.g., III was prepared by N-alkylation of 1,4-dioxa-8-azaspiro[4.5]decane with 6-(4-(chloromethyl)phenyl)-N-((R)-1-phenylethyl)-7H-pyrrolo[2,3-d]pyrimidin-4-amine (preparation given) and deprotection followed by condensation with 6-aminohexanoic acid Me ester and amidation with hydroxylamine. Select I were evaluated in EGFR assays, e.g., III demonstrated an IC50 value of ≤0.1 (μM).
IT 1011716-90-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(preparation of (aralkylamino)(phenyl)pyrrolopyrimidine derivs. for use as protein tyrosine kinase (PTK) inhibitors)

RN 1011716-90-7 CAPLUS

CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[4-[4-[[(1R)-1-phenylethyl]amino]-7H-pyrrolo[2,3-d]pyrimidin-6-yl]phenyl]methyl]-1-piperazinyl]- (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:816930 CAPLUS
DOCUMENT NUMBER: 147:211903
TITLE: Preparation of pyrimidine derivatives as histone deacetylase inhibitors
INVENTOR(S): Marconnet-Decrane, Laurence Francoise Bernadette; Gaurrand, Sandrine Francoise Dominique; Angibaud, Patrick Rene
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 62pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007082874	A1	20070726	WO 2007-EP50371	20070116
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2630717	A1	20070726	CA 2007-2630717	20070116
PRIORITY APPLN. INFO.:			EP 2006-100570 A	20060119
			WO 2007-EP50371 W	20070116
OTHER SOURCE(S):	MARPAT 147:211903			

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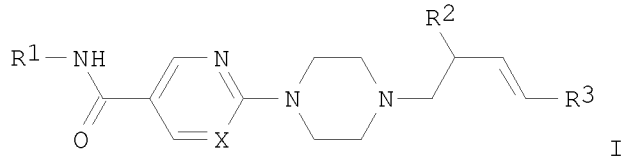

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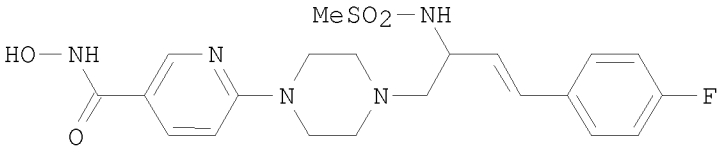

F_3CCO_2H II

<12/04/2007> Erich Leese

AB The title compds. with general formula I [wherein R1 = OH or substituted phenyl; X = N or CH; R2 = amino, alkylamino, alkoxyl, OH, etc.; R3 = (un)substituted Ph, naphthalene, or heterocycle] or N-oxide forms, pharmaceutically acceptable salts, or stereoisomeric forms thereof were prepared as histone deacetylase (HDAC) inhibitors for the treatment of proliferative diseases. For example, compound II was prepared in a multi-step synthesis. In vitro assay for inhibition of HDAC was performed to measure the inhibition of HDAC enzymic activity, and colorimetric assay was performed to determine cellular activity on A2780 tumor cells. II showed HDAC inhibitory and anti-proliferative activities in the above two assays with pIC50 values of 7.0 and 5.3, resp. Formulations containing I as active ingredients were also reported.

IT 944738-91-4P 944738-94-7P 944738-97-0P
944739-00-8P 944739-08-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyrimidine derivs. as histone deacetylase inhibitors)

RN 944738-91-4 CAPLUS

CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-(acetylamino)-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

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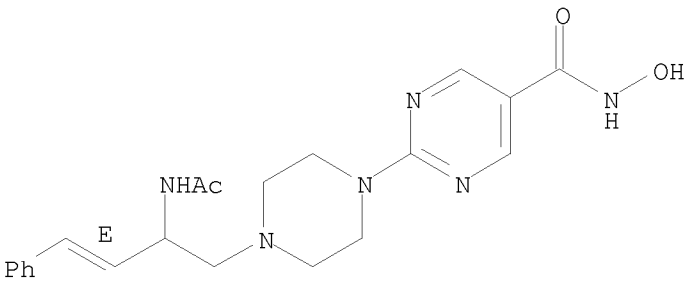
CRN 944738-90-3
CMF C21 H26 N6 O3

Double bond geometry as shown.



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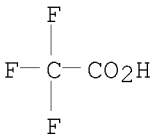
CRN 76-05-1
CMF C2 H F3 O2

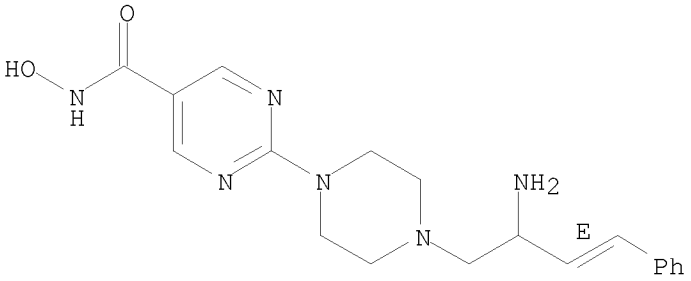


RN 944738-94-7 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-amino-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 944738-93-6
CMF C19 H24 N6 O2

Double bond geometry as shown.



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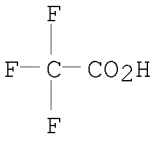
CMF C2 H F3 O2

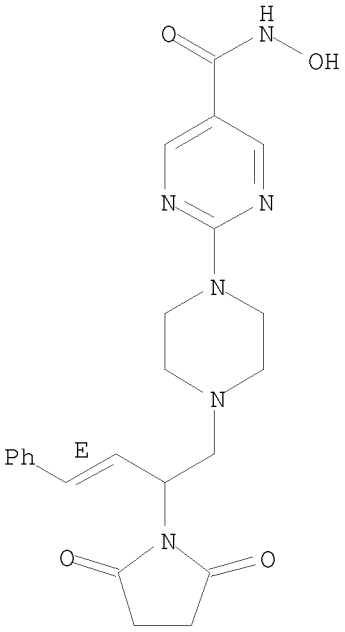


RN 944738-97-0 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-(2,5-dioxo-1-pyrrolidinyl)-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 944738-96-9
CMF C23 H26 N6 O4

Double bond geometry as shown.



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CRN 76-05-1
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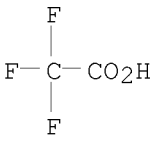

RN 944739-00-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-(4-fluorophenoxy)-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

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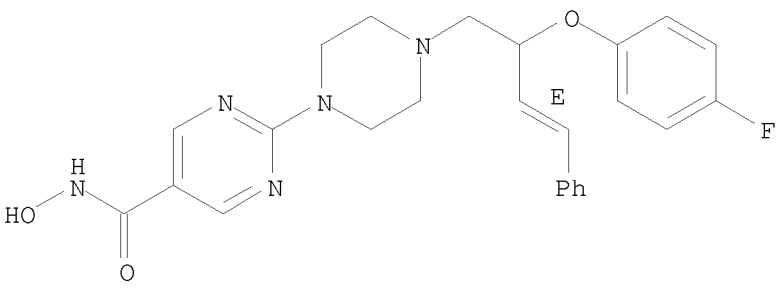
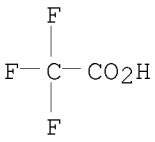
CRN 944738-99-2
CMF C25 H26 F N5 O3

Double bond geometry as shown.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

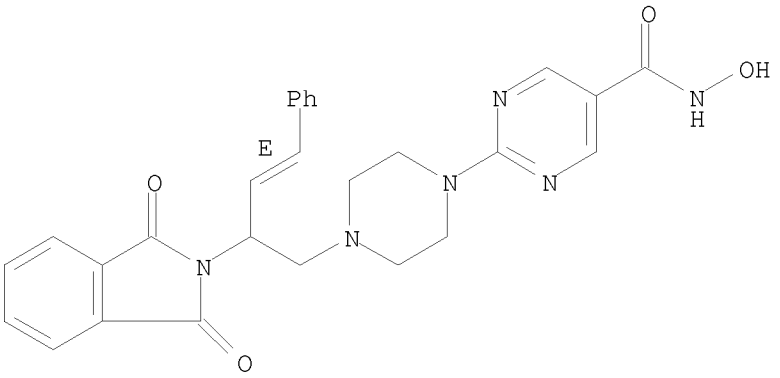


RN 944739-08-6 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(3E)-2-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)-4-phenyl-3-buten-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 944739-07-5
CMF C27 H26 N6 O4

Double bond geometry as shown.



CM 2

CRN 76-05-1
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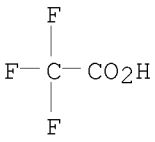

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:816806 CAPLUS
DOCUMENT NUMBER: 147:211902
TITLE: Preparation of pyrimidine derivatives as histone deacetylase inhibitors
INVENTOR(S): Angibaud, Patrick Rene; Van Brandt, Sven Franciscus Anna; Marconnet-Decrane, Laurence Francoise Bernadette; Roux, Bruno
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 63pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007082880	A1	20070726	WO 2007-EP50379	20070116

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: EP 2006-100571 A 20060119
OTHER SOURCE(S): MARPAT 147:211902
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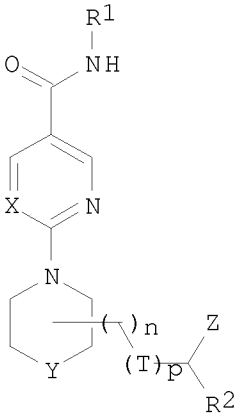

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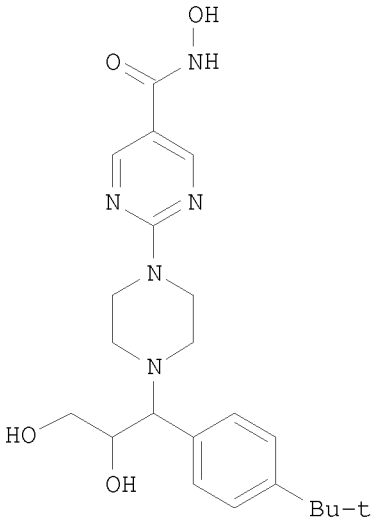

II

AB The title compds. with general formula I [wherein R1 = OH or substituted phenyl; R2 = -CH2OH, -CH2OCH3, -CH2OCH2CH3, or -CH2CH(OH)CH2OH; T = N(R3), where R3 = H, alkyl, cycloalkyl, etc.; X = N or CH; Y = O, NH, CH2, etc.; n = 0-1; p = 0-1, provided that when p = 0 then n = 0 and Y = N, and -CH(R2)-Z is attached to Y; Z = (un)substituted aryl or heteroaryl] or N-oxide forms, pharmaceutically acceptable salts, or stereoisomeric forms thereof were prepared as histone deacetylase (HDAC) inhibitors for the treatment of proliferative diseases. For example, compound II was prepared in a multi-step synthesis. In vitro assay for inhibition of HDAC was performed to measure the inhibition of HDAC enzymic activity, and colorimetric assay was performed to determine cellular activity on A2780 tumor cells. II showed HDAC inhibitory and anti-proliferative activities in the above two assays with pIC50 values of 7.0 and 7.1, resp. Formulations containing I as active ingredients were also reported.

IT 944712-03-2P 944712-05-4P 944712-07-6P
944712-09-8P 944712-10-1P 944712-12-3P
944712-14-5P 944712-16-7P 944712-18-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyrimidine derivs. as histone deacetylase inhibitors)

RN 944712-03-2 CAPLUS

CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[2-hydroxy-1-(1-naphthalenyl)ethyl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 944712-02-1
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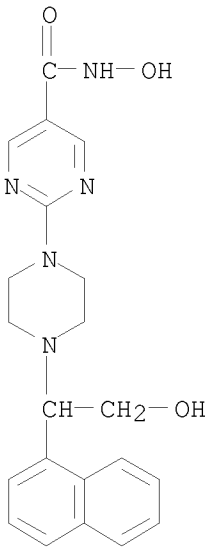
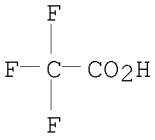


CM 2

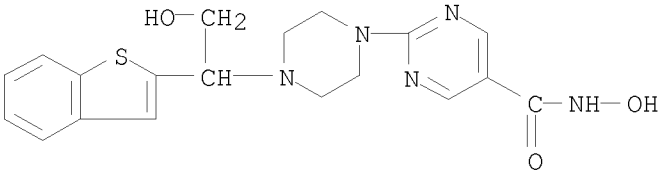
CRN 76-05-1
CMF C2 H F3 O2



RN 944712-05-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-(1-benzo[b]thien-2-yl-2-hydroxyethyl)-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

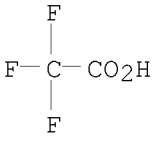
CM 1

CRN 944712-04-3
CMF C19 H21 N5 O3 S



CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 944712-07-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[2-hydroxy-1-[1-(phenylsulfonyl)-1H-indol-3-yl]ethyl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

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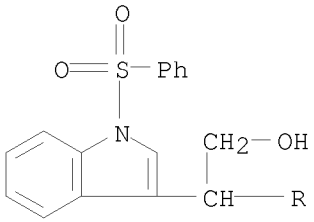
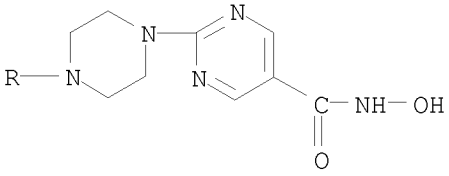
CRN 944712-06-5
CMF C25 H26 N6 O5 S





CM 2

CRN 76-05-1
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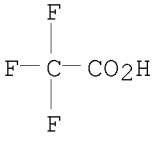
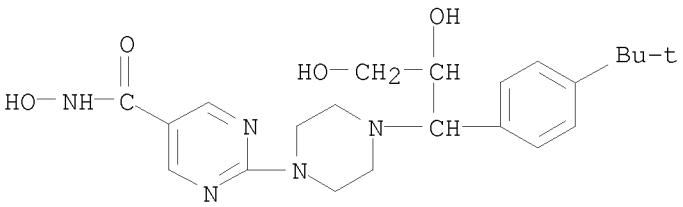


RN 944712-09-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[4-(1,1-dimethylethyl)phenyl]-2,3-

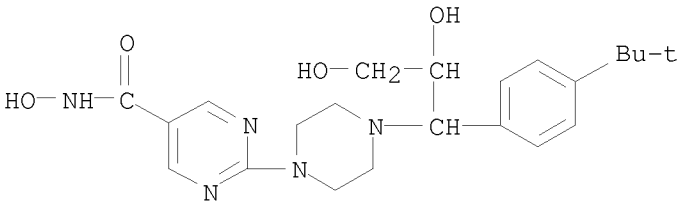
dihydroxypropyl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



RN 944712-10-1 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[4-(1,1-dimethylethyl)phenyl]-2,3-dihydroxypropyl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

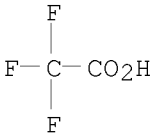
CM 1

CRN 944712-09-8
CMF C22 H31 N5 O4



CM 2

CRN 76-05-1
CMF C2 H F3 O2

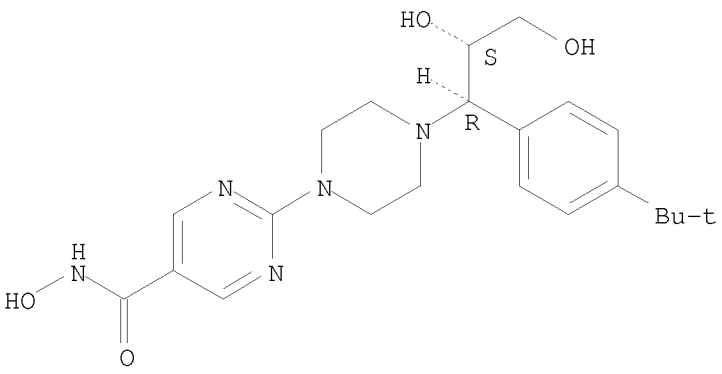


RN 944712-12-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(1R,2S)-1-[4-(1,1-dimethylethyl)phenyl]-2,3-dihydroxypropyl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

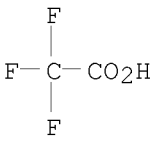
CRN 944712-11-2
CMF C22 H31 N5 O4

Absolute stereochemistry.



CM 2

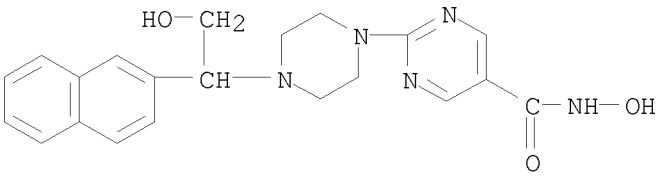
CRN 76-05-1
CMF C2 H F3 O2



RN 944712-14-5 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[2-hydroxy-1-(2-naphthalenyl)ethyl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

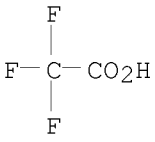
CM 1

CRN 944712-13-4
CMF C21 H23 N5 O3



CM 2

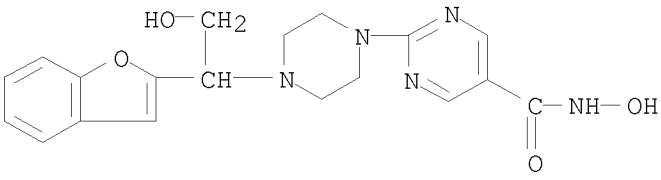
CRN 76-05-1
CMF C2 H F3 O2



RN 944712-16-7 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-(2-benzofuranyl)-2-hydroxyethyl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

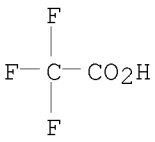
CM 1

CRN 944712-15-6
CMF C19 H21 N5 O4



CM 2

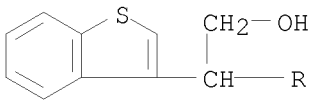
CRN 76-05-1
CMF C2 H F3 O2

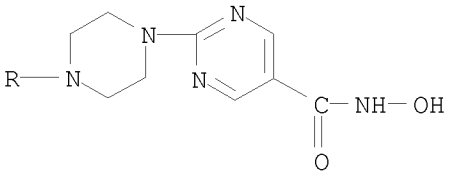


RN 944712-18-9 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-(1-benzo[b]thien-3-yl-2-hydroxyethyl)-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

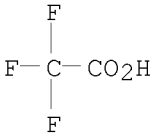
CRN 944712-17-8
CMF C19 H21 N5 O3 S





CM 2

CRN 76-05-1
CMF C2 H F3 O2



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:101446 CAPLUS
DOCUMENT NUMBER: 144:192266
TITLE: Preparation of substituted propenyl piperazine derivatives as novel inhibitors of histone deacetylase
INVENTOR(S): Van Brandt, Sven Franciscus Anna; Van Emelen, Kristof; Angibaud, Patrick Rene; Marconnet-Decrane, Laurence Francoise Bernadette; Arts, Janine
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2006010749	A2	20060202	WO 2005-EP53611		20050725
WO 2006010749	A3	20060608			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
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EP 1776358	A2	20070425	EP 2005-777776		20050725
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CN 1993356	A	20070704	CN 2005-80025487		20050725
JP 2008508234	T	20080321	JP 2007-523072		20050725
BR 2005013891	A	20080520	BR 2005-13891		20050725
KR 2007043978	A	20070426	KR 2007-701641		20070123
US 20070135424	A1	20070614	US 2007-626215		20070123
IN 2007DN00658	A	20070803	IN 2007-DN658		20070124
MX 200701119	A	20070315	MX 2007-1119		20070126
NO 2007001117	A	20070227	NO 2007-1117		20070227
PRIORITY APPLN. INFO.:			EP 2004-77171	A	20040728
			US 2004-592357P	P	20040729
			WO 2005-EP53611	W	20050725

OTHER SOURCE(S): CASREACT 144:192266; MARPAT 144:192266
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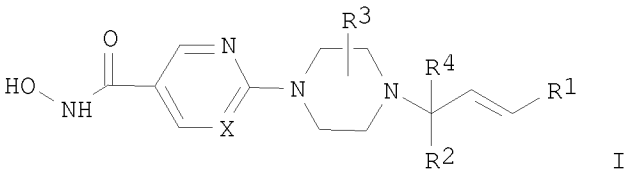

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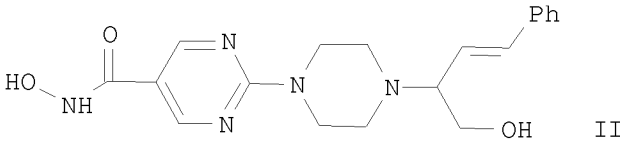

II

AB Substituted propenyl piperazine derivs. I, wherein X is independently N or CH; R1 is Ph, naphthalenyl or heterocyclyl; wherein each of said Ph or naphthalenyl is optionally substituted with one or two substituents each independently selected from halo, alkyl, alkyloxy, poly-halo-alkyl, aryl, hydroxy, cyano, amino, alkylcarbonylamino, alkylsulfonylamino, hydroxycarbonyl, alkyloxycarbonyl, hydroxyalkyl, alkyloxymethyl, aminomethyl, alkylaminomethyl, alkylcarbonylaminomethyl, alkylsulfonylaminomethyl, aminosulfonyl, alkylaminosulfonyl or heterocyclyl; R2 is hydrogen, -CH2R5, trifluoromethyl, -C(O)-R6, or -CH-NR7R8; wherein each R5 is independently hydrogen, hydroxy, alkyloxy, alkyloxyalkyloxy, alkylcarbonyloxy, piperazinyl, N-methylpiperazinyl, morpholinyl, thiomorpholinyl, imidazolyl or triazolyl; each R6 is independently hydroxy, alkyloxy, amino or mono- or di(alkyl)amino, cycloalkylamino, hydroxyalkylamino, piperazinyl, N-methylpiperazinyl, morpholinyl or thiomorpholinyl; each R7 and R8 are independently hydrogen, alkyl, alkylcarbonyl, alkylsulfonyl, or mono- or di(alkyl)aminosulfonyl; R3 is hydrogen, hydroxymethyl, aminomethyl or mono- or di(alkyl)aminomethyl; R4 is hydrogen or alkyl; were prepared and having histone deacetylase inhibiting enzymic activity and to inhibit proliferative conditions, such as cancer and psoriasis. Thus, propenyl piperazine derivative II was prepared and tested in vitro and in nude mice as inhibitor of histone deacetylase and was better than R306465 after oral administration. P21 enzyme linked immunosorbent assay has been applied to determine the p21 protein expression level in human A2780 ovarian carcinoma cells. In vitro assay for inhibition of histone deacetylase is reported. P21 induction was measured as the consequence of DNA damage or as the consequence of histone deacetylase inhibition. Antiproliferative activity of title compds. was determined on A2780 cells (neg. log value of the IC50, pIC50 = 7.9-8.2).

IT 875138-85-5P 875138-87-7P 875138-88-8P
875138-89-9P 875138-90-2P 875138-91-3P
875138-93-5P 875138-94-6P 875138-98-0P
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875139-06-3P 875139-07-4P 875139-09-6P
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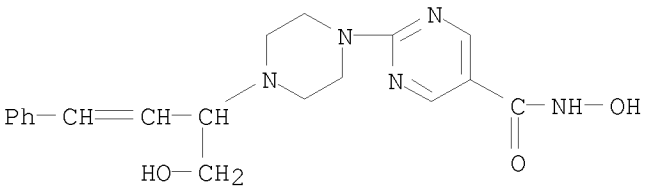
875139-27-8P 875139-28-9P 875139-29-0P
875139-30-3P 875139-31-4P 875139-69-8P

875139-70-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted propenyl piperazine derivs. as novel inhibitors of histone deacetylase)

RN 875138-85-5 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(hydroxymethyl)-3-phenyl-2-propen-1-yl]-1-piperazinyl]- (CA INDEX NAME)



RN 875138-87-7 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3-(4-chlorophenyl)-1-(4-morpholinylmethyl)-2-propen-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 875138-86-6
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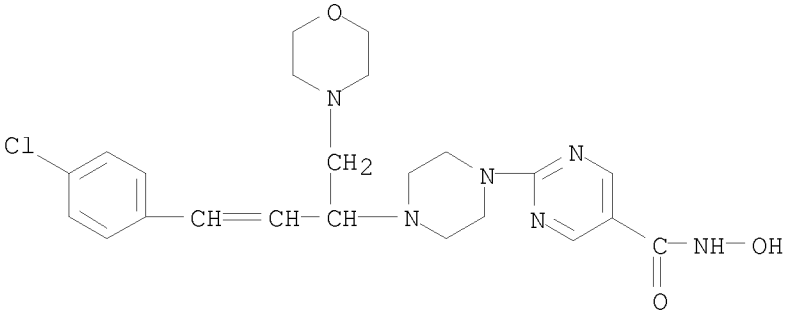
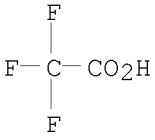


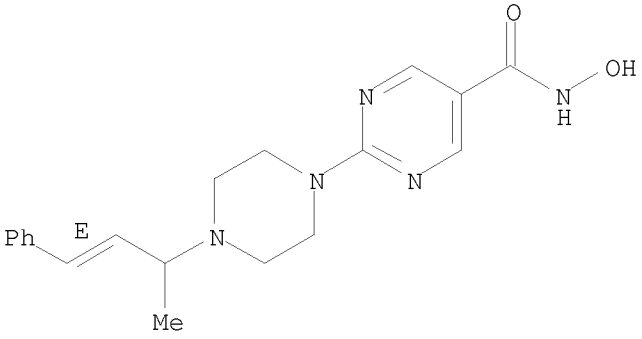
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 875138-88-8 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(2E)-1-methyl-3-phenyl-2-propen-1-yl]-1-piperazinyl]- (CA INDEX NAME)

Double bond geometry as shown.

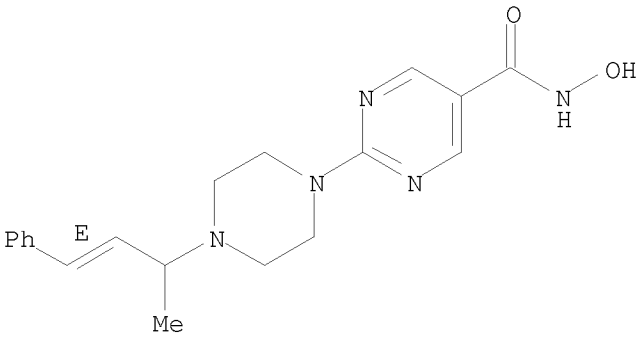


RN 875138-89-9 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(2E)-1-methyl-3-phenyl-2-propen-1-yl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

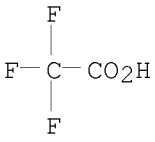
CRN 875138-88-8
CMF C19 H23 N5 O2

Double bond geometry as shown.

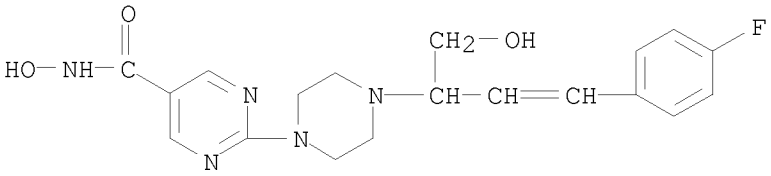


CM 2

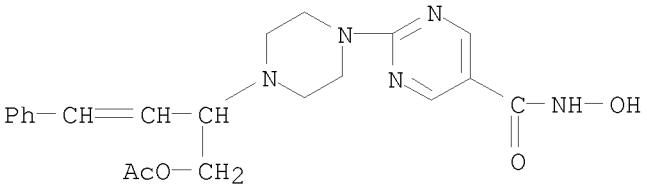
CRN 76-05-1
CMF C2 H F3 O2



RN 875138-90-2 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3-(4-fluorophenyl)-1-(hydroxymethyl)-2-propen-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



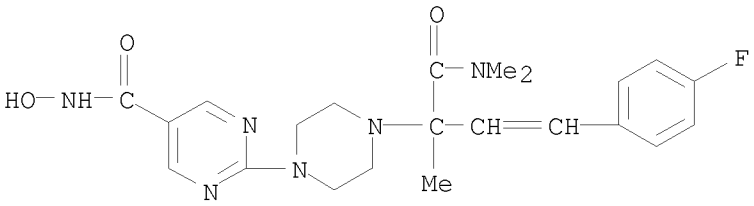
RN 875138-91-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[(acetyloxy)methyl]-3-phenyl-2-propen-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



RN 875138-93-5 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[(dimethylamino)carbonyl]-3-(4-fluorophenyl)-1-methyl-2-propen-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

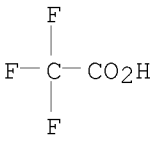
CM 1

CRN 875138-92-4
CMF C22 H27 F N6 O3

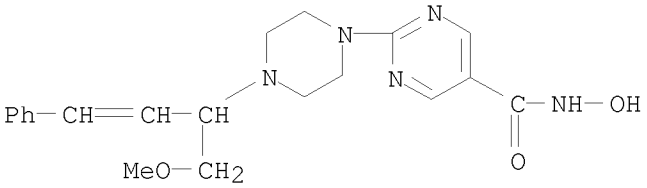


CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 875138-94-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(methoxymethyl)-3-phenyl-2-propen-1-yl]-1-piperazinyl]- (CA INDEX NAME)

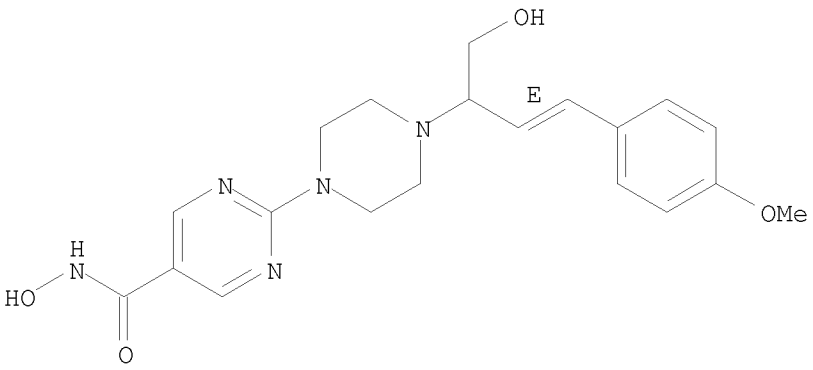


RN 875138-98-0 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(2E)-1-(hydroxymethyl)-3-(4-methoxyphenyl)-2-propen-1-yl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 875138-97-9
CMF C20 H25 N5 O4

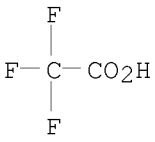
Double bond geometry as shown.



CM 2

CRN 76-05-1

CMF C2 H F3 O2

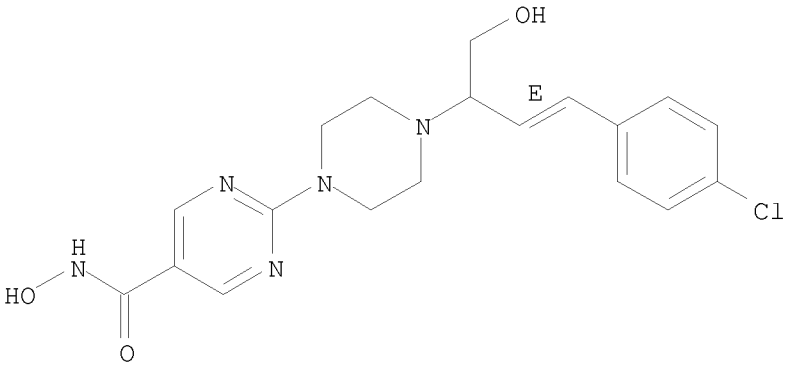


RN 875139-00-7 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(2E)-3-(4-chlorophenyl)-1-(hydroxymethyl)-2-propen-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

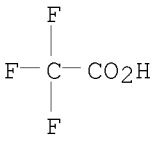
CRN 875138-99-1
CMF C19 H22 Cl N5 O3

Double bond geometry as shown.



CM 2

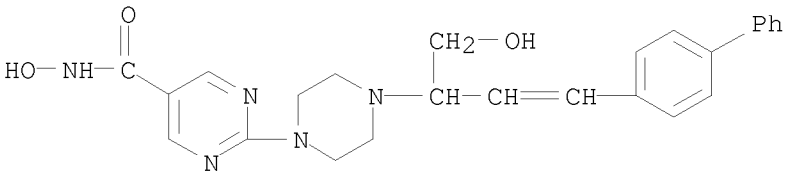
CRN 76-05-1
CMF C2 H F3 O2



RN 875139-02-9 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3-[1,1'-biphenyl]-4-yl-1-(hydroxymethyl)-2-propen-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

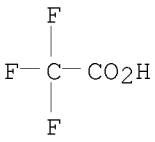
CM 1

CRN 875139-01-8
CMF C25 H27 N5 O3



CM 2

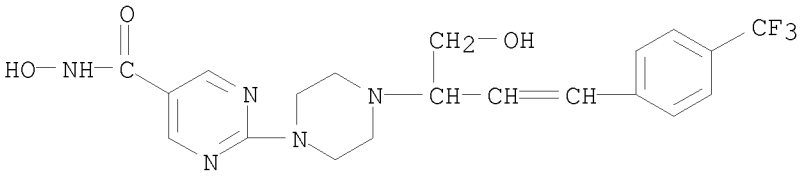
CRN 76-05-1
CMF C2 H F3 O2



RN 875139-04-1 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(hydroxymethyl)-3-[4-(trifluoromethyl)phenyl]-2-propen-1-yl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

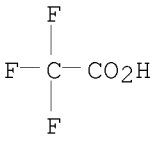
CM 1

CRN 875139-03-0
CMF C20 H22 F3 N5 O3



CM 2

CRN 76-05-1
CMF C2 H F3 O2

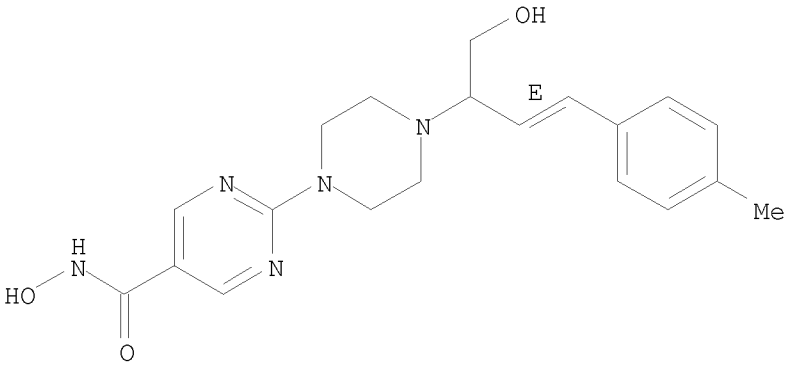


RN 875139-06-3 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(2E)-1-(hydroxymethyl)-3-(4-methylphenyl)-2-propen-1-yl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

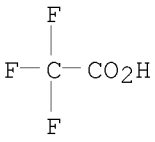
CRN 875139-05-2
CMF C20 H25 N5 O3

Double bond geometry as shown.

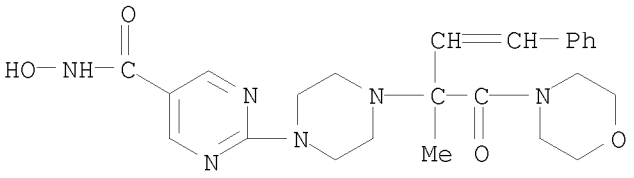


CM 2

CRN 76-05-1
CMF C2 H F3 O2



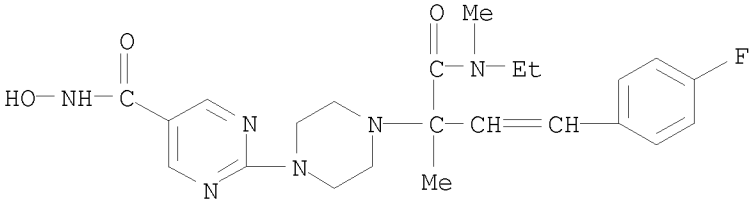
RN 875139-07-4 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-methyl-1-(4-morpholinylcarbonyl)-3-phenyl-2-propen-1-yl]-1-piperazinyl]- (CA INDEX NAME)



RN 875139-09-6 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[(ethylmethylamino)carbonyl]-3-(4-fluorophenyl)-1-methyl-2-propen-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

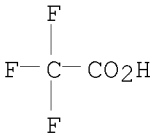
CM 1

CRN 875139-08-5
CMF C23 H29 F N6 O3



CM 2

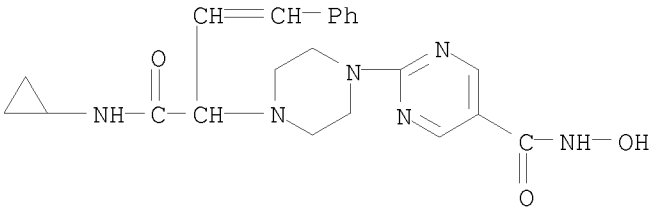
CRN 76-05-1
CMF C2 H F3 O2



RN 875139-11-0 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[(cyclopropylamino)carbonyl]-3-phenyl-2-propen-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

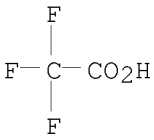
CM 1

CRN 875139-10-9
CMF C22 H26 N6 O3



CM 2

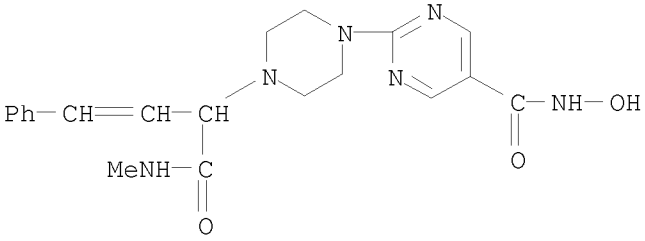
CRN 76-05-1
CMF C2 H F3 O2



RN 875139-13-2 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-[(methylamino)carbonyl]-3-phenyl-2-propen-1-yl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

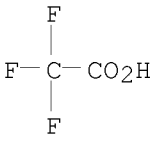
CM 1

CRN 875139-12-1
CMF C20 H24 N6 O3

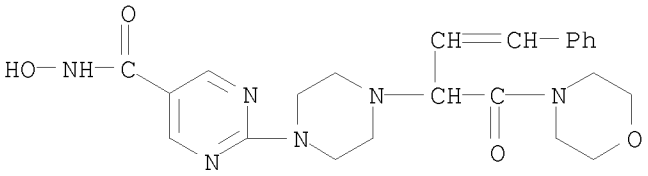


CM 2

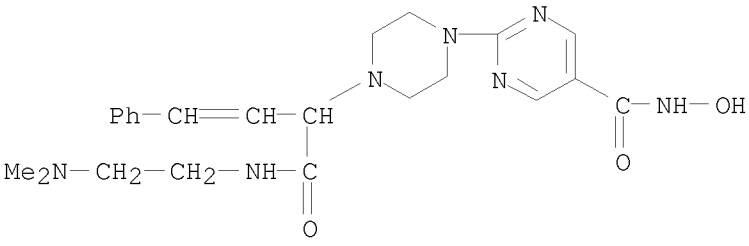
CRN 76-05-1
CMF C2 H F3 O2



RN 875139-14-3 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(4-morpholinylcarbonyl)-3-phenyl-2-propen-1-yl]-1-piperazinyl]- (CA INDEX NAME)



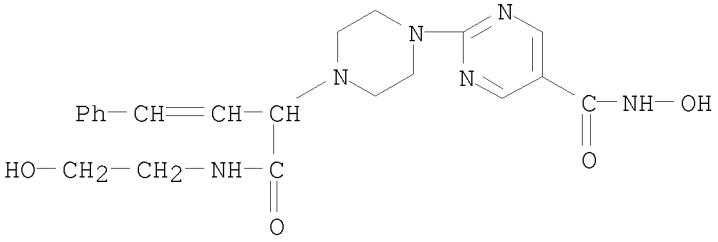
RN 875139-15-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[[[2-(dimethylamino)ethyl]amino]carbonyl]-3-phenyl-2-propen-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



RN 875139-17-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-[[(2-hydroxyethyl)amino]carbonyl]-3-phenyl-2-propen-1-yl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

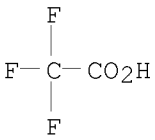
CM 1

CRN 875139-16-5
CMF C21 H26 N6 O4



CM 2

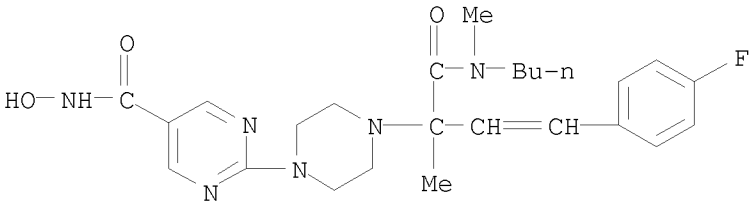
CRN 76-05-1
CMF C2 H F3 O2



RN 875139-19-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-[(butylmethylamino)carbonyl]-3-(4-fluorophenyl)-1-methyl-2-propen-1-yl]-1-piperazinyl]-N-hydroxy-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

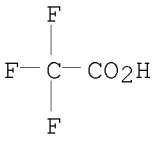
CM 1

CRN 875139-18-7
CMF C25 H33 F N6 O3

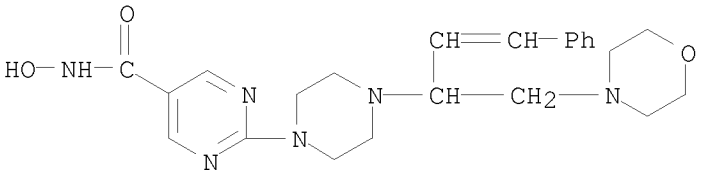


CM 2

CRN 76-05-1
CMF C2 H F3 O2

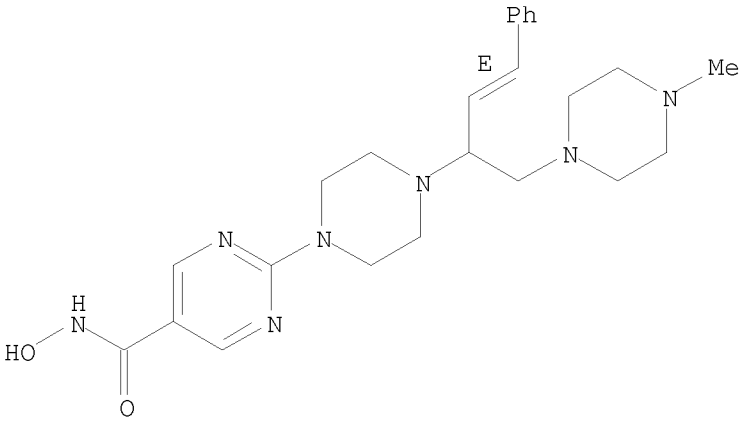


RN 875139-20-1 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(4-morpholinylmethyl)-3-phenyl-2-propen-1-yl]-1-piperazinyl]- (CA INDEX NAME)



RN 875139-21-2 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(2E)-1-[(4-methyl-1-piperazinyl)methyl]-3-phenyl-2-propen-1-yl]-1-piperazinyl]- (CA INDEX NAME)

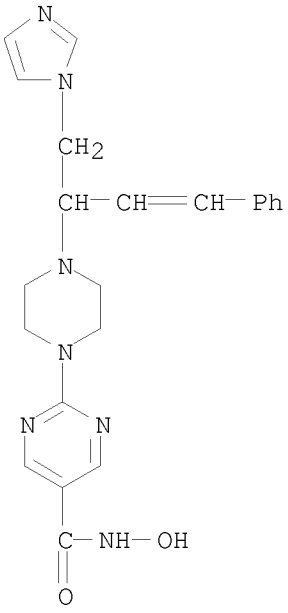
Double bond geometry as shown.



RN 875139-23-4 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[1-(1H-imidazol-1-ylmethyl)-3-phenyl-2-propen-1-yl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

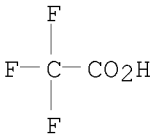
CM 1

CRN 875139-22-3
CMF C22 H25 N7 O2

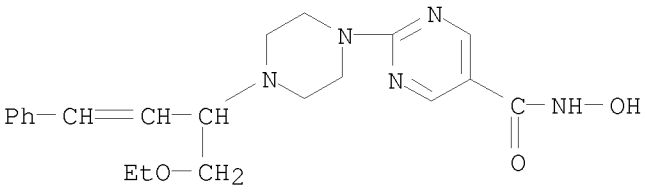


CM 2

CRN 76-05-1
CMF C2 H F3 O2



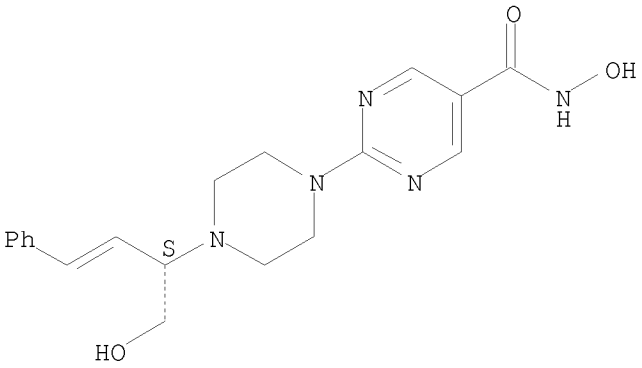
RN 875139-24-5 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[1-(ethoxymethyl)-3-phenyl-2-propen-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



RN 875139-25-6 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(1S)-1-(hydroxymethyl)-3-phenyl-2-propen-1-yl]-1-piperazinyl]- (CA INDEX NAME)

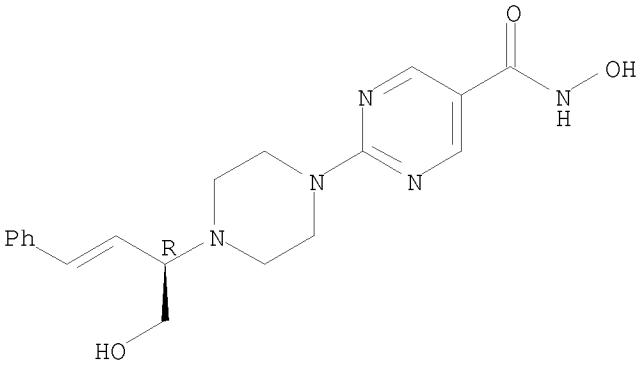
Absolute stereochemistry.

Double bond geometry unknown.



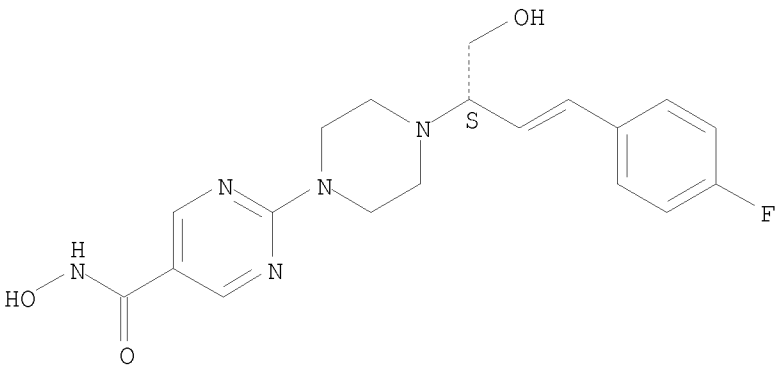
RN 875139-26-7 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[(1R)-1-(hydroxymethyl)-3-phenyl-2-propen-1-yl]-1-piperazinyl]- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

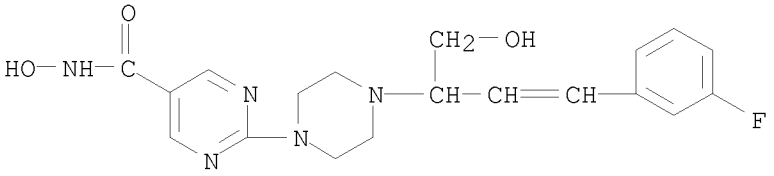


RN 875139-27-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(1S)-3-(4-fluorophenyl)-1-(hydroxymethyl)-2-propen-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)

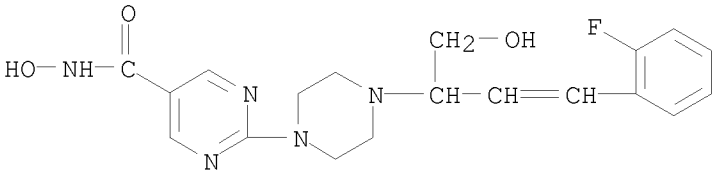
Absolute stereochemistry.
Double bond geometry unknown.



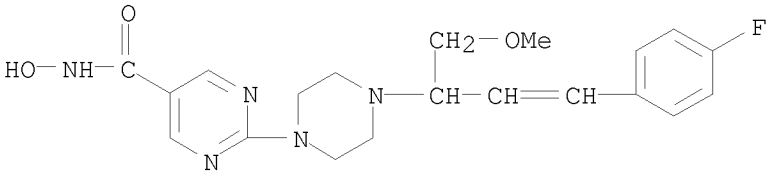
RN 875139-28-9 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3-(3-fluorophenyl)-1-(hydroxymethyl)-2-propen-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



RN 875139-29-0 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3-(2-fluorophenyl)-1-(hydroxymethyl)-2-propen-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



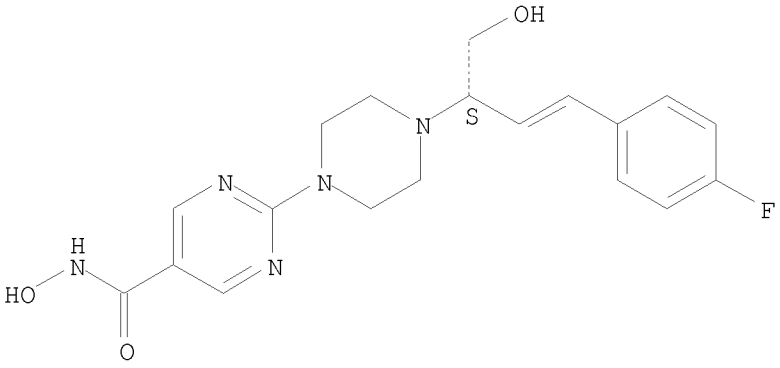
RN 875139-30-3 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[3-(4-fluorophenyl)-1-(methoxymethyl)-2-propen-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



RN 875139-31-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(1S)-3-(4-fluorophenyl)-1-(hydroxymethyl)-2-

propen-1-yl]-1-piperazinyl]-N-hydroxy-, hydrochloride (1:1) (CA INDEX NAME)

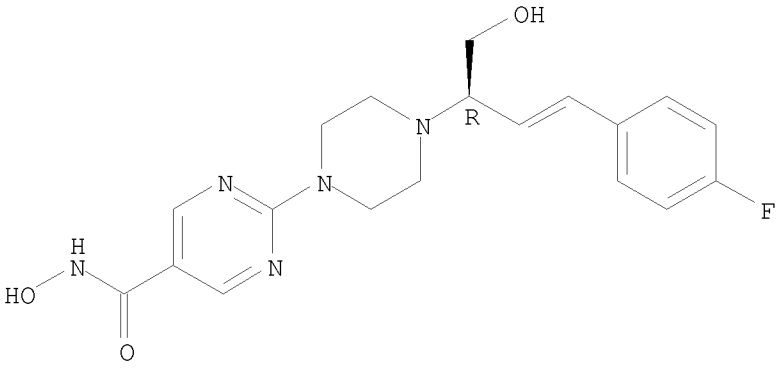
Absolute stereochemistry.
Double bond geometry unknown.



● HCl

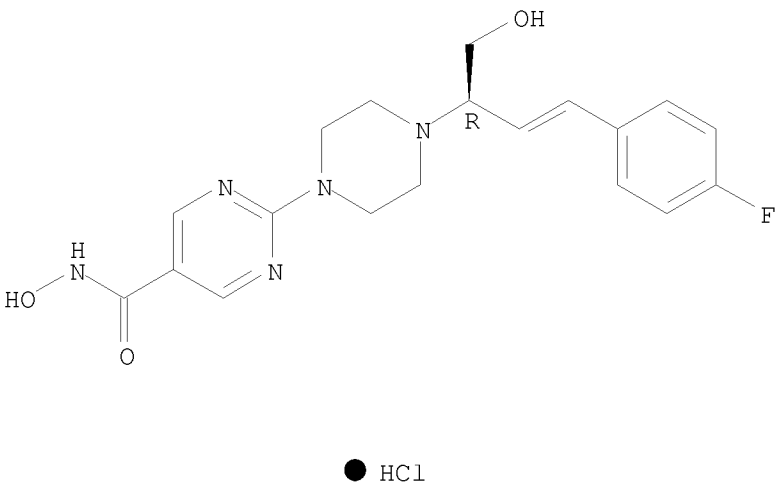
RN 875139-69-8 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(1R)-3-(4-fluorophenyl)-1-(hydroxymethyl)-2-propen-1-yl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 875139-70-1 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[(1R)-3-(4-fluorophenyl)-1-(hydroxymethyl)-2-propen-1-yl]-1-piperazinyl]-N-hydroxy-, hydrochloride (1:1) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



● HCl

L14 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:300395 CAPLUS
DOCUMENT NUMBER: 142:355054
TITLE: Preparation of amide derivatives as inhibitors of histone deacetylase
INVENTOR(S): Moradei, Oscar; Paquin, Isabelle; Leit, Silvana; Frechette, Sylvie; Vaisburg, Arkadii; Besterman, Jeffrey M.; Tessier, Pierre; Mallais, Tammy C.
PATENT ASSIGNEE(S): Methylgene, Inc., Can.
SOURCE: PCT Int. Appl., 559 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2005030705	A1	20050407	WO 2004-US31591		20040924
WO 2005030705	A9	20060420			
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
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CA 2539117	A1	20050407	CA 2004-2539117		20040924
EP 1663953	A1	20060607	EP 2004-789074		20040924
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CN 1882529	A	20061220	CN 2004-80034571		20040924
JP 2007506785	T	20070322	JP 2006-528279		20040924
US 20080132459	A1	20080605	US 2006-574088		20060323
JP 2008094847	A	20080424	JP 2007-281356		20071030
PRIORITY APPLN. INFO.:			US 2003-505884P	P	20030924
			US 2003-532973P	P	20031229
			US 2004-561082P	P	20040409
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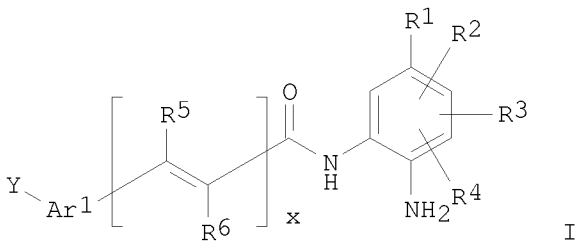
			WO 2004-US31591	W	20040924

OTHER SOURCE(S): CASREACT 142:355054; MARPAT 142:355054
GI



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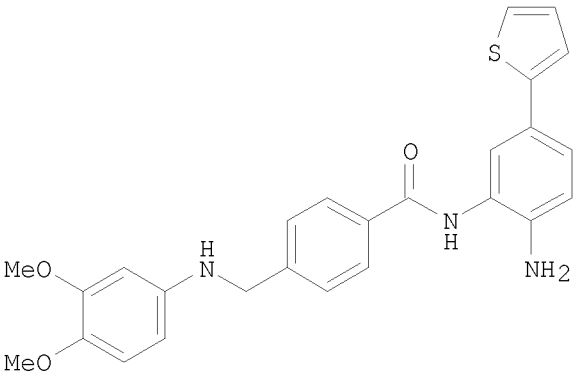


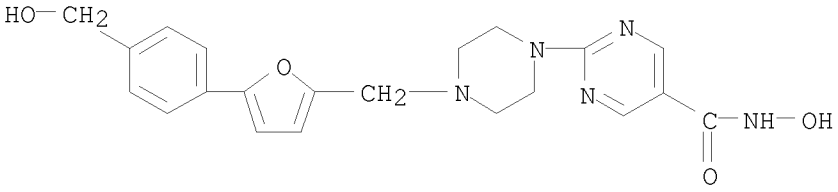
II

AB Title compds. I [Ar1 = (un)saturated-, (un)substituted-mono or fused poly-cyclic hydrocarbyl optionally containing 1-4 heteroatoms per ring; R1 = (un)substituted-mono-, -bi-, -tri-cyclic-aryl or -heteroaryl; R2, R3, and R4 independently = H, halo, amino, etc.; R5 and R6 independently = H, alkyl, aryl, etc.; x = 0-1; Y = any pharmaceutically acceptable chemical moiety consisting of 1 to 50 atoms with provisions] and their pharmaceutically acceptable salts, are prepared and disclosed as inhibitors of histone deacetylase. Thus, e.g., II was prepared by Suzuki coupling of 2-bromo-2-nitro-phenylamine (preparation given) with 2-thiopheneboronic acid followed by carbonylation with 4-[3,4-dimethoxy-(phenylamino)-methyl]benzoic acid (preparation given) and subsequent reduction The inhibitory capability of I towards antiproliferative activity of histone deacetylase enzyme was evaluated using 3-[4,5-dimethylthiazol-2-yl-2,5-diphenyltetrazolium] bromide (MTT) assay and it revealed that certain compds. of the invention had MTT IC 50 values in the range of below 1 up to 20 μM. I as histone deacetylase inhibitors should prove useful in the treatment of diseases such as, but not limited to, cell proliferative disease, protozoal disease, and fungal disease.

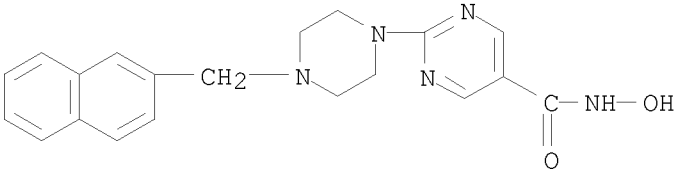
IT 603985-86-0P 603985-88-2P 603985-90-6P
603985-94-0P 603991-95-3P 603991-96-4P
603992-24-1P 603992-25-2P 603992-26-3P
603992-27-4P 603992-28-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amide derivs. as inhibitors of histone deacetylase)

RN 603985-86-0 CAPLUS

CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[5-[4-(hydroxymethyl)phenyl]-2-furanyl]methyl]-1-piperazinyl]- (CA INDEX NAME)



RN 603985-88-2 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-naphthalenylmethyl)-1-piperazinyl]- (CA INDEX NAME)



RN 603985-90-6 CAPLUS
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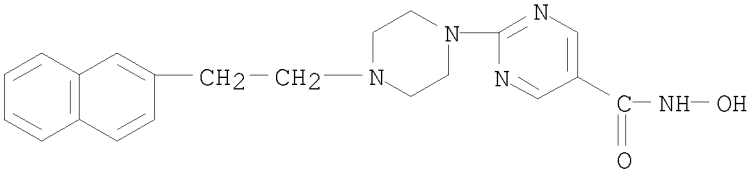

RN 603985-94-0 CAPLUS
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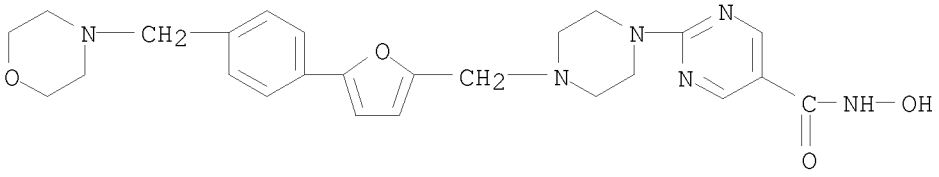

RN 603991-95-3 CAPLUS
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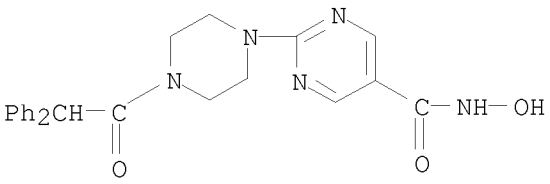

RN 603991-96-4 CAPLUS
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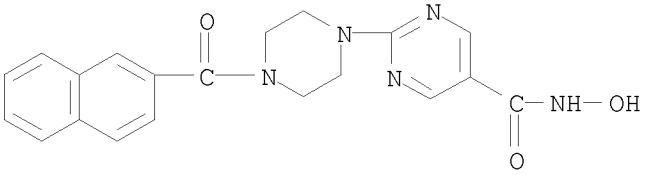

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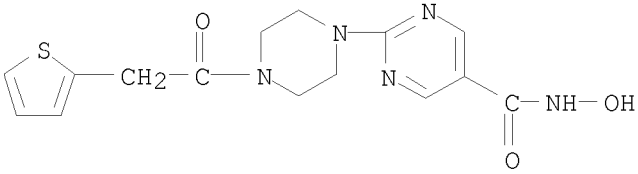

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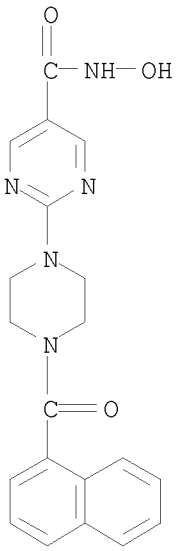

RN 603992-26-3 CAPLUS
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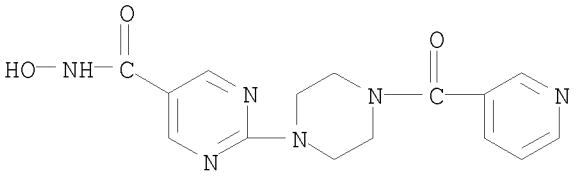

RN 603992-27-4 CAPLUS
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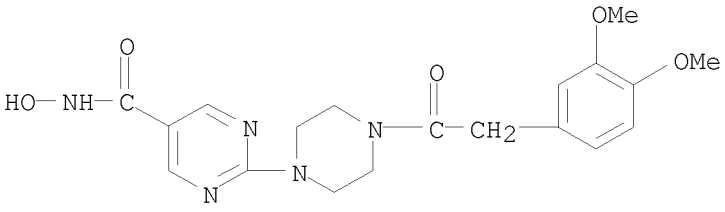
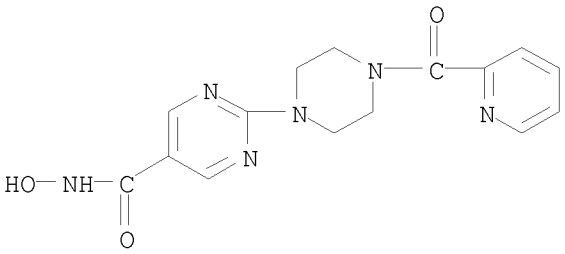


RN 603992-28-5 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-pyridinylcarbonyl)-1-piperazinyl]- (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:300394 CAPLUS
DOCUMENT NUMBER: 142:373563
TITLE: Preparation of amide derivatives as inhibitors of histone deacetylase
INVENTOR(S): Moradei, Oscar; Paquin, Isabelle; Leit, Silvana; Frechette, Sylvie; Vaisburg, Arkadii; Besterman, Jeffrey M.; Tessier, Pierre; Mallais, Tammy C.
PATENT ASSIGNEE(S): Methylgene, Inc., Can.
SOURCE: PCT Int. Appl., 389 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2005030704	A1	20050407	WO 2004-US31590		20040924
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
JP 2008094847	A	20080424	JP 2007-281356		20071030
PRIORITY APPLN. INFO.:			US 2003-505884P	P	20030924
			US 2003-532973P	P	20031229
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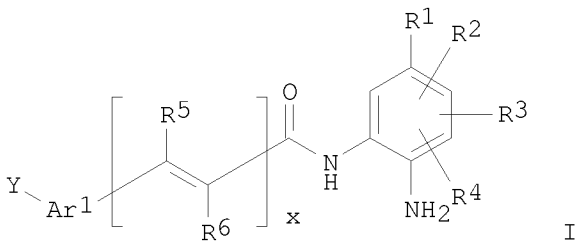
			JP 2006-528279	A3	20040924

OTHER SOURCE(S): CASREACT 142:373563; MARPAT 142:373563
GI



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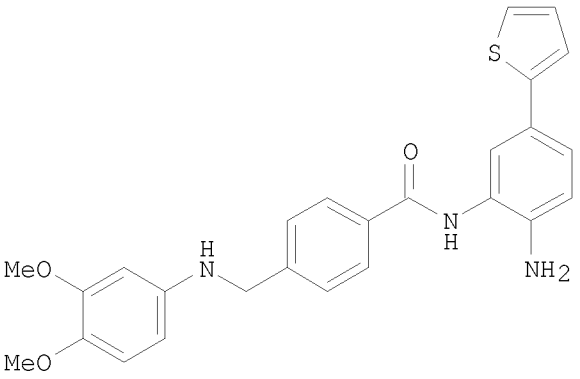

II

AB Title compds. I [Ar1 = (un)saturated-, (un)substituted-mono or fused poly-cyclic hydrocarbyl optionally containing 1-4 heteroatoms per ring; R1 = (un)substituted-mono-, -bi-, -tri-cyclic-aryl or -heteroaryl; R2, R3, and R4 independently = H, halo, amino, etc.; R5 and R6 independently = H, alkyl, aryl, etc.; x = 0-1; Y = any pharmaceutically acceptable chemical moiety consisting of 1 to 50 atoms with provisions] and their pharmaceutically acceptable salts, are prepared and disclosed as inhibitors of histone deacetylase. Thus, e.g., II was prepared by Suzuki coupling of 2-bromo-2-nitro-phenylamine (preparation given) with 2-thiopheneboronic acid followed by carbonylation with 4-[3,4-dimethoxy-(phenylamino)-methyl]benzoic acid (preparation given) and subsequent reduction The inhibitory capability of I towards antiproliferative activity of histone deacetylase enzyme was evaluated using 3-[4,5-dimethylthiazol-2-yl-2,5-diphenyltetrazolium] bromide (MTT) assay and it revealed that certain compds. of the invention had MTT IC 50 values in the range of below 1 up to 20 μM. I as histone deacetylase inhibitors should prove useful in the treatment of diseases such as, but not limited to, cell proliferative disease, protozoal disease, and fungal disease.

IT 603985-86-0P 603985-88-2P 603985-90-6P
603985-94-0P 603991-95-3P 603991-96-4P
603992-24-1P 603992-25-2P 603992-26-3P
603992-27-4P 603992-28-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amide derivs. as inhibitors of histone deacetylase)

RN 603985-86-0 CAPLUS

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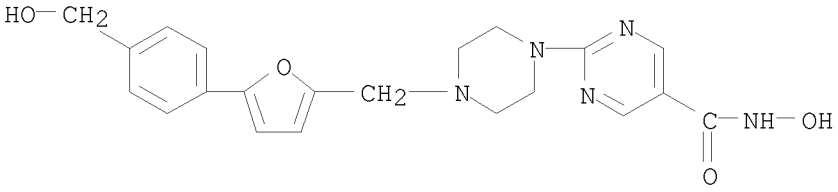

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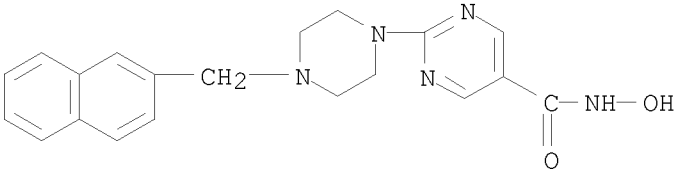

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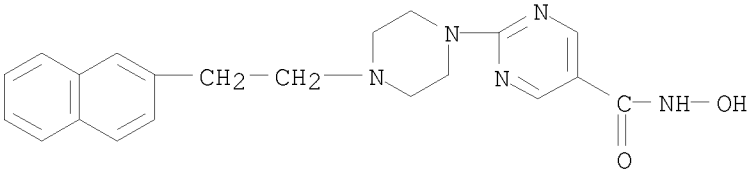
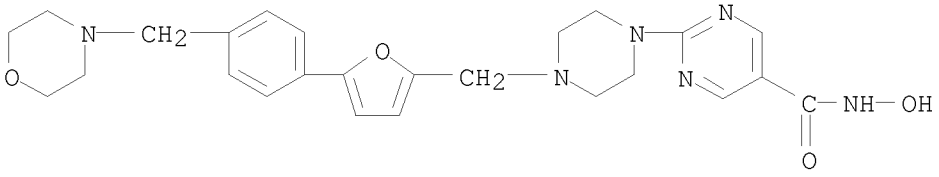


RN 603985-94-0 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[5-[4-(4-morpholinylmethyl)phenyl]-2-furanyl]methyl]-1-piperazinyl]- (CA INDEX NAME)



RN 603991-95-3 CAPLUS
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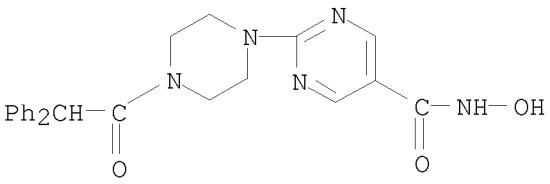

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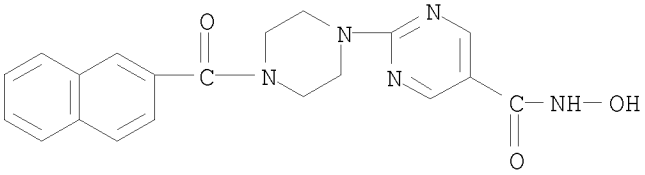

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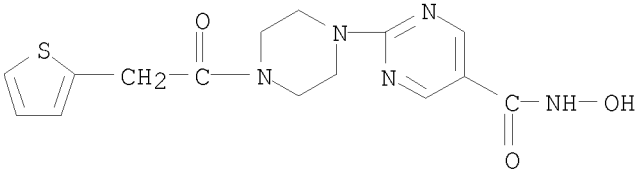
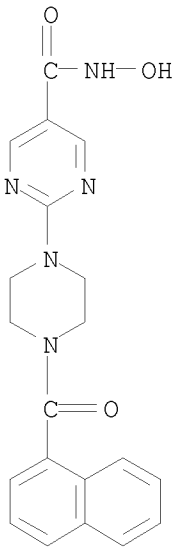


RN 603992-25-2 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(1-naphthalenylcarbonyl)-1-piperazinyl]- (CA INDEX NAME)



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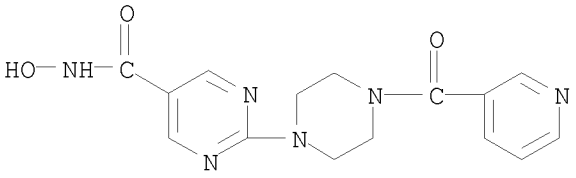
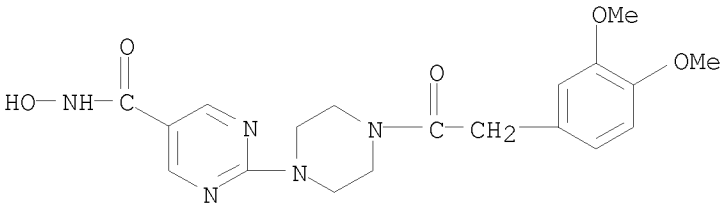
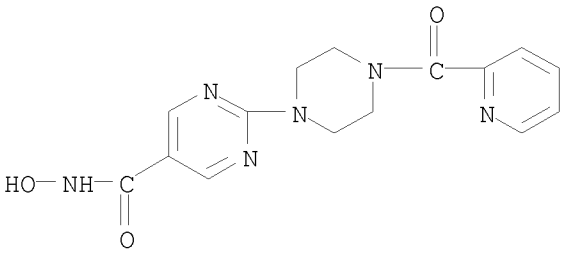


RN 603992-27-4 CAPLUS
CN 5-Pyrimidinecarboxamide, 2-[4-[2-(3,4-dimethoxyphenyl)acetyl]-1-piperazinyl]-N-hydroxy- (CA INDEX NAME)



RN 603992-28-5 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-pyridinylcarbonyl)-1-piperazinyl]- (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:737723 CAPLUS
DOCUMENT NUMBER: 139:261309
TITLE: Preparation of N-hydroxy-5-piperazino(piperidino or diazepino)-2-pyrimidinecarboxamides and N-hydroxy-4-piperazino(piperidino or diazepino)benzamides as new inhibitors of histone deacetylase
INVENTOR(S): Angibaud, Patrick Rene; Pilatte, Isabelle Noeelle Constance; Van Brandt, Sven Franciscus Anna; Roux, Bruno; Ten Holte, Peter; Verdonck, Marc Gustaaf Celine; Meerpoel, Lieven; Dyatkin, Alexey Borisovich
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076400	A1	20030918	WO 2003-EP2514	20030311
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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AU 2003218736	A1	20030922	AU 2003-218736	20030311
EP 1485353	A1	20041215	EP 2003-711980	20030311
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CN 1639125	A	20050713	CN 2003-805675	20030311
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CN 101007803	A	20070801	CN 2007-10005212	20030311
IN 2004DN02533	A	20070413	IN 2004-DN2533	20040831
US 20050107384	A1	20050519	US 2004-506998	20040908
ZA 2004007237	A	20050928	ZA 2004-7237	20040909
ZA 2004007235	A	20051004	ZA 2004-7235	20040909
ZA 2004007232	A	20051006	ZA 2004-7232	20040909
ZA 2004007233	A	20051006	ZA 2004-7233	20040909
ZA 2004007234	A	20051006	ZA 2004-7234	20040909
ZA 2004007236	A	20051006	ZA 2004-7236	20040909
MX 2004PA08806	A	20041126	MX 2004-PA8806	20040910
NO 2004004194	A	20041001	NO 2004-4194	20041001
PRIORITY APPLN. INFO.:			US 2002-363799P P	20020313
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			CN 2003-805921 A3	20030311

WO 2003-EP2514 W 20030311

OTHER SOURCE(S): MARPAT 139:261309

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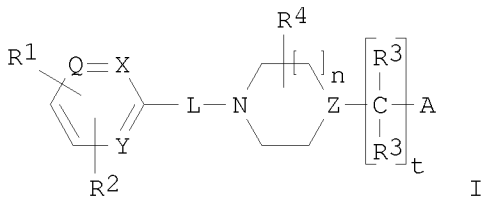

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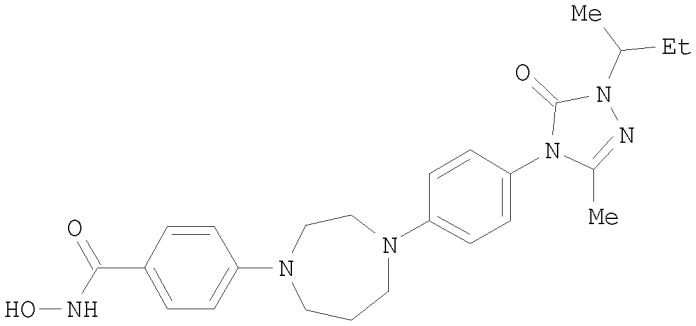

II

AB The title compds. [I; n = 0-3; t = 0-4; Q, X, Y = N, C; Z = N, CH; R1 = CONR7R8, NHCOR9, CO(alkanediyl)SR9, etc. (wherein R7, R8 = H, OH, alkyl, etc.; R9 = H, alkyl, alkylcarbonyl, etc.); R2 = H, halo, OH, etc.; L = a bond, alkanediyl, alkanediyloxy, NH, CO, NHCO; each R3 = H and one H atom can be replaced by aryl; R4 = H, OH, NH2, etc.; A = (un)substituted Ph, cyclohexyl, pyridyl, etc.], having histone deacetylase inhibiting enzymic activity, were prepared and formulated. E.g., a multi-step synthesis of II which showed pIC50 of 5.121 against HDAC, was given.

IT 603985-87-1P 603985-89-3P 603985-91-7P
603985-95-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazino(piperidino or diazepino) substituted 2-pyrimidinecarbohydroxamic acids and N-hydroxybenzamides as new inhibitors of histone deacetylase)

RN 603985-87-1 CAPLUS

CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[5-[4-(hydroxymethyl)phenyl]-2-furanyl]methyl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (5:4) (CA INDEX NAME)

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CRN 603985-86-0
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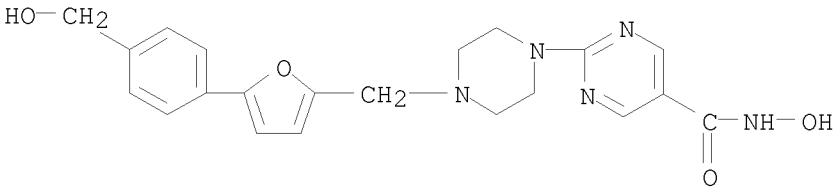

CM 2

CRN 76-05-1
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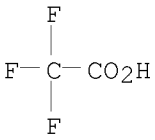

RN 603985-89-3 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-naphthalenylmethyl)-1-piperazinyl]-, 2,2,2-trifluoroacetate (5:4) (CA INDEX NAME)

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CRN 603985-88-2
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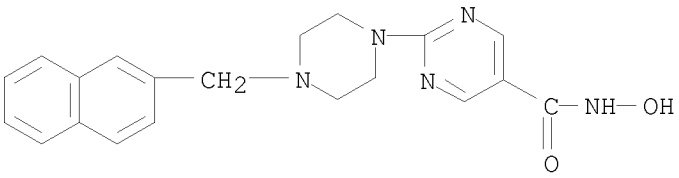

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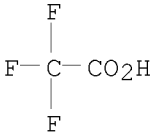

RN 603985-91-7 CAPLUS

CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[2-(2-naphthalenyl)ethyl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (5:4) (CA INDEX NAME)

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CRN 603985-90-6
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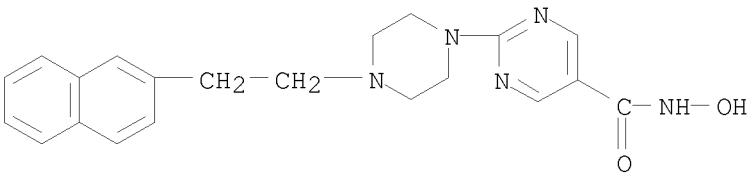

CM 2

CRN 76-05-1
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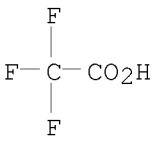

RN 603985-95-1 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[[5-[4-(4-morpholinylmethyl)phenyl]-2-furanyl]methyl]-1-piperazinyl]-, 2,2,2-trifluoroacetate (1:2) (CA INDEX NAME)

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CRN 603985-94-0
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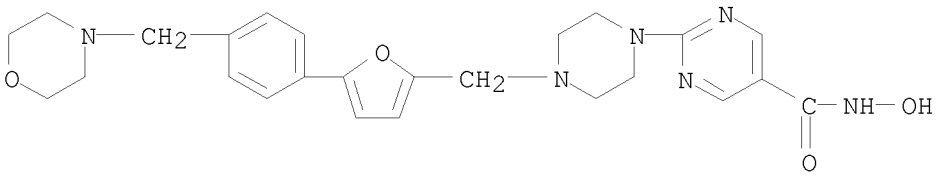

CM 2

CRN 76-05-1
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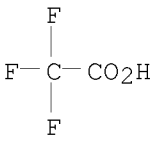

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:737586 CAPLUS
DOCUMENT NUMBER: 139:261308
TITLE: Preparation of aryl and heteroaryl hydroxamic acids as inhibitors of histone deacetylase for treating proliferative diseases
INVENTOR(S): Van Emelen, Kristof; Verdonck, Marc Gustaaf Celine; Van Brandt, Sven Franciscus Anna; Angibaud, Patrick Rene; Meerpoel, Lieven; Dyatkin, Alexey Borisovich
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003075929	A1	20030918	WO 2003-EP2515		20030311
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2476065	A1	20030918	CA 2003-2476065		20030311
AU 2003218737	A1	20030922	AU 2003-218737		20030311
AU 2003218737	B2	20080410			
EP 1485099	A1	20041215	EP 2003-711981		20030311
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003007624	A	20050111	BR 2003-7624		20030311
CN 1639125	A	20050713	CN 2003-805675		20030311
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JP 2005525379	T	20050825	JP 2003-574203		20030311
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CN 101007803	A	20070801	CN 2007-10005212		20030311
IN 2004DN02537	A	20070112	IN 2004-DN2537		20040831
ZA 2004007237	A	20050928	ZA 2004-7237		20040909
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US 20050096468	A1	20050505	US 2004-507785		20040913
NO 2004004113	A	20040928	NO 2004-4113		20040928
PRIORITY APPLN. INFO.:			US 2002-363799P	P	20020313
			WO 2002-EP14833	A	20021223
			CN 2003-805921	A3	20030311
			WO 2003-EP2515	W	20030311

OTHER SOURCE(S): MARPAT 139:261308

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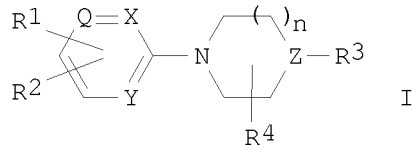

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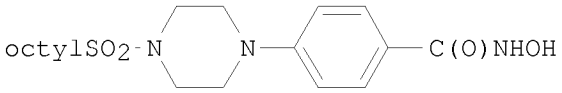


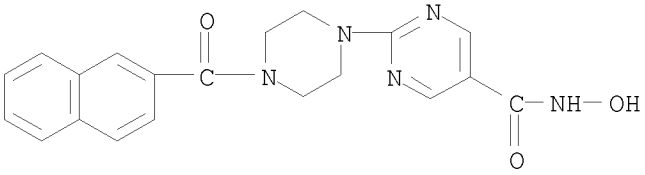
II

AB This invention comprises aryl and heteroaryl hydroxamic acids (shown as I; variables defined below; e.g. II) having histone deacetylase inhibiting enzymic activity; their preparation, compns. containing them and their use as a medicine. Compds. I show excellent in-vitro histone deacetylase inhibiting enzymic activity, have advantageous properties with regard to cellular activity and specific properties with regard to inhibition of cell cycle progression at both G1 and G2 checkpoints (p21 induction capacity), and show good metabolic stability and high bioavailability and more particular show oral bioavailability. They can also be used for detection and identification of histone deacetylase. General synthetic procedures and characterization data for twenty-seven I are included; also, prepns. of 12 intermediates are included. For example, a 59 % yield of 2-[4-(dimethylaminosulfonyl)piperazin-1-yl]pyrimidine-5-carbohydroxamic acid was obtained by removing the O-tetrahydropyranyl group of its ester using trifluoroacetic acid; the ester was prepared in 61 % yield from N'-(ethylcarbonimidoyl)-N,N-dimethyl-1,3-propanediamine monohydrochloride, sodium 2-[4-(dimethylaminosulfonyl)piperazin-1-yl]pyrimidine-5-carboxylate, O-(tetrahydro-2H-pyran-2-yl)hydroxylamine, and 1-hydroxy-1H-benzotriazole in CH2Cl2/THF. The sodium salt was obtained by base hydrolysis of the Et ester; the ester was prepared in 73 % yield from Et 2-(piperazin-1-yl)pyrimidine-5-carboxylate and dimethylsulfamoyl chloride; Et 2-(piperazin-1-yl)pyrimidine-5-carboxylate was obtained in <96 % yield from Et 2-(4-benzylpiperazin-1-yl)pyrimidine-5-carboxylate by hydrogenation using Pd/C; the benzyl derivative was obtained from 1-(phenylmethyl)piperazine, (135 mL) was added gradually to a solution of potassium carbonate (0.18 mol) and 2-(methylsulfonyl)-5-pyrimidinecarboxylic acid Et ester, K2CO3 in MeCN. For I: n is 0-3; Q, X and Y are N or C; Z is N or CH; R1 is -C(O)NR5R6, -N(H)C(O)R7, -C(O)-C1-6alkanediylSR7, -NR8C(O)N(OH)R7, -NR8C(O)C1-6alkanediylSR7, -NR8C(O)C:N(OH)R7 or another Zn-chelating-group; R2 is H, halo, hydroxy, amino, nitro, C1-6alkyl, C1-6alkyloxy, trifluoromethyl, di(C1-6-alkyl)amino, hydroxyamino or naphthalenylsulfonylpyrazinyl. R3 is H, C1-6-alkyl, arylC2-6alkenediyl, furanylcarbonyl, naphthalenylcarbonyl, -C(O)phenylR9, C1-6alkylaminocarbonyl, aminosulfonyl, arylaminosulfonyl, aminosulfonylamino, di(C1-6-alkyl)aminosulfonylamino, arylaminosulfonylamino, aminosulfonylaminoC1-6-alkyl, di(C1-6-alkyl)aminosulfonylaminoC1-6-alkyl, arylaminosulfonylaminoC1-6alkyl, di(C1-6-alkyl)aminoC1-6alkyl, Cl1-12-alkylsulfonyl, di(C1-6-alkyl)aminosulfonyl, trihaloC1-6-alkylsulfonyl, di(aryl)C1-6alkylcarbonyl, thiophenylC1-6alkylcarbonyl, pyridinylcarbonyl or arylC1-6alkylcarbonyl. R4 is H, hydroxy, amino, hydroxyC1-6alkyl, C1-6alkyl, C1-6alkyloxy,

arylC1-6alkyl, aminocarbonyl, hydroxycarbonyl, aminoC1-6-alkyl, aminocarbonylC1-6-alkyl, hydroxycarbonylC1-6-alkyl, hydroxyaminocarbonyl, C1-6-alkyloxycarbonyl, C1-6-alkylaminoC1-6-alkyl or di(C1-6-alkyl)aminoC1-6-alkyl; when R3 and R4 are present on the same C atom, R3 and R4 together may form -C(O)-NH-CH2-NR10- wherein R10 is H or aryl; when R3 and R4 are present on adjacent C atoms, R3 and R4 together may form :CH-CH:CH-CH: ; addnl. details are given in the claims.

IT 603991-96-4P
RL: ARG (Analytical reagent use); PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate and reagent for detection/identification of histone deacetylase; preparation of aryl and heteroaryl hydroxamic acids as inhibitors of histone deacetylase for treating proliferative diseases)

RN 603991-96-4 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-(2-naphthalenylcarbonyl)-1-piperazinyl]- (CA INDEX NAME)



IT 603991-95-3P 603992-24-1P 603992-25-2P
603992-26-3P 603992-27-4P 603992-28-5P
RL: ARG (Analytical reagent use); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate and reagent for detection/identification of histone deacetylase; preparation of aryl and heteroaryl hydroxamic acids as inhibitors of histone deacetylase for treating proliferative diseases)

RN 603991-95-3 CAPLUS
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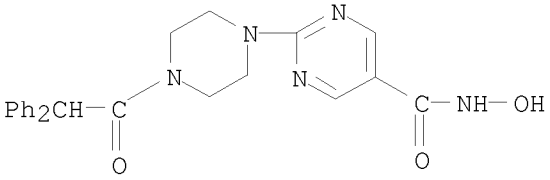

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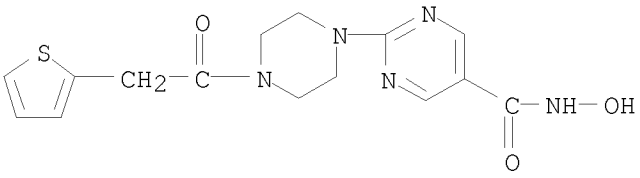

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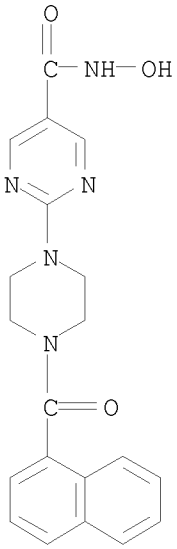

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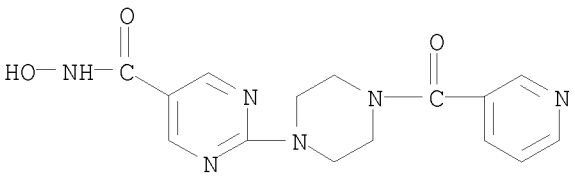

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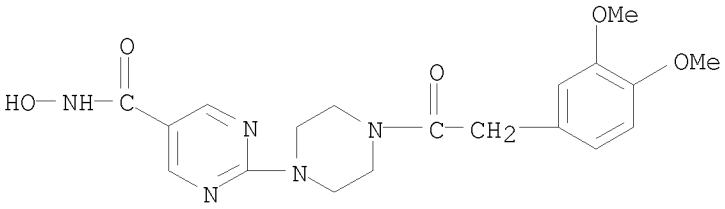

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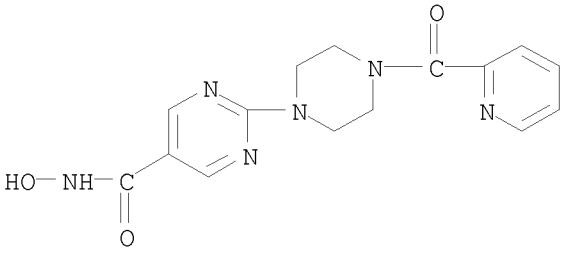

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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